A RETROSPECTIVE COST ANALYSIS INVESTIGATION OF THE EXTENSIVE DRUG RESISTANT TUBERCULOSIS TREATMENT AT THE CHURCH OF SCOTLAND AND KING GEORGE HOSPITALS IN KWAZULU-NATAL, SOUTH AFRICA

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ABSTRACT

The emergence of resistant forms of tuberculosis (TB) has not only caused continuous challenges on the world populations' health, but has also attracted increased costs of primary health care for the infected and society at large. In 2005, when the South African public came to learn about another resistant form of TB other than multi-drug resistant (MDR), 53 patients had just died in a rural hospital in KwaZulu-Natal (KZN). The reports (SA DoH, 2006) came to announce this form of TB as extreme drug resistant tuberculosis (XDR-TB).

Since the emergence of XDR-TB in South Africa, the concern around treatment cost were highlighted in the South African Health ministry's reports. It was reported that in 2006 the medical cost of treating a patient with ordinary TB was around R 400.00 per month. Costs escalated if patients defaulted on treatment and developed a MDR-TB with cost of treatment increasing to around R 24,000.00 per month inclusive of hospitalisation and more expensive drugs (SA DoH, 2006). These costs can only increase, considering that the treatment is for a longer period, with a more expensive drug regimen, and a very low success rate.

Study reports have shown a link between resistant TB forms and the human immunodeficiency virus/acquired immunity deficiency syndrome (HIV/AIDS) epidemic. High morbidity rates that result from this link will ultimately create a financial challenge for the health system. It is because of such a challenge that the financial implications that the new strain poses, and its consequences if not contained, or controlled, need to be assessed.

The purpose of the study was to establish the financial implications that the resistant form(s) of TB will have at the study site, King George Hospital (KGH) in KZN. KGH was selected as a study site because it is the central institution of XDR-TB coordination in KZN province where the first cases were reported. KGH also serves as the referral hospital for TB cases in the province. Church of Scotland Hospital (CoSH) frequently uses KGH for referral. The motivation to conduct such a study was based on understanding how much public resources will be utilised to treat an XDR-TB patient at the sites. When HIV was first discovered in the 1980's, it was never envisaged that billions of rand would be spent treating HIV infected sufferers. It is possible to get to that point with XDR-TB.

This retrospective study had a sample size of 156 subjects in the co-infected group cohort (both HIV and XDR-TB infections in one host) 106 of the 143, that is 74.13% tested positive for HIV. The study design included patients that were in hospital for treatment (inpatients), as well as those that had been treated on a continuous basis as out-patients. Investigated parameters were both medical and non-medical for both groups. For hospitalised patients, the patient day equivalent (PDE) cost calculation considered the public health facility's resource allocation. PDE cost

encompassed the total daily costs to the hospital of caring for a patient (Thomas *et al.*, 2007). PDE formula was useful as a tool to summarize the average patient daily treatment expenditure, and consideration in the formula was made to distinguish inpatients, out-patients and day patients as costs vary (HST, 2009).

Results from this study indicated that the investigated medical and non-medical costs were directly proportional to both hospital stay and days on treatment. Rates differed based on the patient's hospital stay arrangements (hospitalised vs. out-patient). Various medical tests performed also attracted costs for the hospitalised patients, as some were routinely done with each week or month of hospitalisation (Rajbhandary *et al.*, 2004).

The study sample had a patient daily equivalent cost ranging from R 1,502.00 in 2002 to R 3,481.00 in 2007. For a 30 day stay in hospital, costs to actively treat and house an XDR-TB patient at KGH were R 77,404.00 in 2002 and escalated to R 144,221.00 in 2007 in real terms.

From this study, it is recommended that the government fast track the process of setting up HIV/AIDS and TB clinics to combat both illnesses in a coordinated manner, and improve healthcare facilities in order to accommodate large numbers of patients to reduce the spread of an airborne TB and it's resistant forms. It is also recommended that the co-infected be separated from the uninfected until such time that the TB and its resistant forms have been cured.

This study provides an indication of the burden on public health resources that XDR-TB can have if the disease is not adequately contained. More money will be required to treat XDR-TB, and compromise will have to be made over other healthcare priorities should budget allocations be insufficient.

DECLARATION

I, Lebogang Molobi, declare that this research report is my own work. It is being submitted for examination in part fulfillment for the degree of Master of Science in Medicine (Pharmaceutical Affairs) at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree at this or any other University.

Signed by:

_____

LEBOGANG MOLOBI (ID: 791110 5189 08 9)

On this…….. Day of ……, 2013

DEDICATION

To my late grandparents Mr. & Mrs. MOLOBI;
You would be proud of the man I have become.

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I would like to convey my sincere appreciation to the many people who have contributed towards this research, either professionally or personally, providing me with the strength to persevere.

To the Lord Almighty, without whom all things are not possible.

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LIST OF ABBREVIATIONS & GLOSSARY

3 I's	-	Intensified case finding, Infection control and Izoniazid prevention therapy
AIDS	-	Acquired Immunity Deficiency Syndrome
ANOVA	-	Analysis of variants
ART	-	Anti-Retroviral Therapy
BCG	-	Bacille Calmette-Guerin vaccine
CDC	-	Center for Disease Control and Prevention (United States)
CoSH	-	Church of Scotland Hospital
CPI	-	Consumer Price Index
Day Patient	-	Patients in hospital for a day for observation and assigned a bed, and can go home with or without treatment or medication
DC	-	District Centers
DoH	-	Department of Health (South Africa)
DOTS	-	Directly Observed Therapy, Short Course
EMRS	-	Emergency Medical Rescue Services
FLD	-	First Line Drugs
FSU	-	Former Soviet Union countries
FV	-	Future Value
HCW	-	HealthCare Worker
HIV	-	Human Immunodeficiency Virus
Inpatient	-	Patients staying overnight in the hospital for further observation
KGH	-	King George Hospital
KZN	-	KwaZulu-Natal province
MDG	-	Millennium Development Goal (United Nations)
MDR-TB	-	Multidrug Resistant Tuberculosis
MSc	-	Master of Science Degree
NPV	-	Net Present Value
Out-patient	-	Patients allowed to go home with treatment or medication
PDE	-	Patient Daily Equivalence
PV	-	Present Value
SA	-	South Africa
SLD	-	Second Line Drugs
SS	-	Sum of Squares
TB	-	Tuberculosis
WHO	-	World Health Organisation
XDR-TB	-	Extreme/Extensive Drug Resistance Tuberculosis

CHAPTER 1

1. INTRODUCTION

1.1 GENERAL OVERVIEW (WORLDWIDE PERSPECTIVE ON TUBERCULOSIS)

1.1.1 Tuberculosis, Multi-Drug Resistant and Extreme Drug Resistant Tuberculosis

Tuberculosis (TB) is a treatable condition caused by *Mycobacterium tuberculosis,* a bacillus that affects the respiratory system with debilitating symptoms of night sweats, weight loss and breakdown in the immune system (SA DoH, 2003).

The spread of TB in the world including South Africa (SA) has seen an emergence of a resistant form during the 1990s called “multi-drug resistant tuberculosis” (MDR-TB), which is defined as resistance of the bacterium to isoniazid and rifampicin, known as first line drugs (FLDs). In the event of an MDR-TB infection the treatment required is the use of second-line drugs (SLDs) which are often less effective, more toxic, and costlier than the first-line isoniazid-and-rifampicin based regimen (Wright *et al.*, 2006). FLDs combine the greatest level of efficacy with an acceptable degree of toxicity, and may include ethambutol, streptomycin, pyrazinamide in addition to isoniazid and rifampicin. SLDs include ofloxacin, ciprofloxacin, ethionamide, aminosalicylic acid, cycloserine, amikacin, kanamycin, and capreomycin (Master, 2009). The use of both SLDs and FLDs agents does not guarantee success against resistant strains.

Extensive drug resistance tuberculosis (or extreme drug resistance tuberculosis, XDR-TB) is a multi-drug resistant tuberculosis that does not respond to isoniazid and rifampicin, and at least 3 of the 6 SLDs (CDC, 2006; MRC, 2006; SA DoH, 2006; Stephenson, 2006 and Wright *et al.*, 2006). The description of XDR-TB was first used in 2006, following a joint survey by World Health Organization (WHO) and the US Center for Disease Control and Prevention (CDC) from Wright *et al.* (2006).

MDR- and XDR-TB are essentially resistant forms caused by man due to lack of compliance to treatment. Exposure to a single drug, whether as a result of poor adherence to treatment, inappropriate prescription, irregular drug supply or poor drug quality, suppresses the growth of *Mycobacterium tuberculosis* susceptible to that drug but permits the multiplication of pre-existing drug-resistant mutants. The patient then develops acquired resistance (Frazer *et al*., 2006).

On average, there are 8 million new cases reported worldwide per year, and a minimum of 2 million deaths caused by ordinary TB (Cummings, 2007; Konaidze *et al.*, 2009; Mathema

et al., 2006; Mu *et al.*, 2009; Munro *et al.*, 2007; Reed *et al.*, 2009 and Smith, 2003). The resistant form of TB such as MDR-TB is documented in over 90 countries worldwide (Munro *et al.*, 2007).

In the South African context the emergence of XDR-TB in 2004 claimed 54 lives, and 347 patients were diagnosed positive. These statistics are a concern considering that SA is struggling with controlling the spread of HIV, and the emergence of XDR-TB is a further financial constraint on the health budget (Ghandhi *et al.*, 2006 and Shah *et al.*, 2007).

1.1.2 Tuberculosis, Multi-Drug Resistant, Extreme Drug Resistant Tuberculosis and Industrialisation

The history of TB, which has now progressed to the resistant forms such as XDR-TB, dates back to 1882 when Robert Koch made a remarkable discovery that TB was caused by an infectious agent, *Mycobacterium tuberculosis* as reported by Mathema *et al.* (2006).

The battle with TB, (even with advancement in technology in modern day world), has not been completely won, as many countries in Europe and Africa are still faced with the challenge to eradicate the disease among its citizens. The challenges in both continents are somewhat different as in some European countries exposure to tobacco inhalation is cited, among others, as a problem by increasing the risk of developing TB, and whereas in African countries, living conditions are seen as a major a problem (Aspler *et al.*, 2008 and Chiang *et al.*, 2007).

The industrialised and developing countries both have challenges of TB eradication, although the nature of their problems is different. Industrialised countries have problems that are easily contained and manageable. Most countries identified young adult immigrants as the cause of continuous increase in TB incidence. A study conducted in Germany from 2004 - 2006 reported 4,557 culture-positive TB cases. Nearly 90% of the participants were immigrants from Former Soviet Union (FSU) countries (Dye, 2006; Eker, 2008; Kik *et al.*, 2009; Kobaidze *et al.*, 2009; Porco *et al.*, 2006; Schwartzman and Menzies, 2000).

Developing countries, mostly in Sub-Saharan Africa (will henceforth be referred to as Africa) still account for most of the TB incidence, with challenges that often differ from industrialised nations (Aspler *et al.*, 2008).

Africa has numerous challenges such as:

a) The environment, with a warm climate that is conducive to the growth of most microorganisms;
b) Lack of finance to secure resources such as healthy diet (Smith, 2003);
c) Infrastructure constraints (Smith, 2003);
d) HIV/AIDS epidemic and various reasons leading to drug resistance as a result of compliance due to erratic drug supply (Smith, 2003);
e) Healthcare provider conduct, with lack of patient respect from nursing personnel (Marra *et al.*, 2004 and Munro *et al.*, 2007);
f) Lack of infection control and
g) Shortage of healthcare workers, in public institutions especially in rural areas (Havlir *et al.*, 2008)

The incidence of HIV/AIDS associated tuberculosis in Africa is hundreds of times more than that in the industrialised world, but the ratio of healthcare workers to population are a tenth of European levels (Corbett *et al.*, 2006). The staff shortage leads to a weakened healthcare system with minimal health intervention programs, such as “Stop TB” campaigns, and ultimately results in high morbidity and mortality rates.

The World Health Organisation (WHO) studied all challenges in treating TB, and in the 1990s developed the Directly Observed Therapy, Short Course (DOTS) strategy which emphasises the diagnoses and treatment of sputum smear-positive, to reduce the mortality and infectiousness related to such cases (Corbett *et al.*, 2006; Day *et al.*, 2004 and WHO, 2009).

The DOTS strategy allowed for compliance monitoring through supervision of 2 months initial treatment phase, up to 6 months for new treatment and 8 months for retreatment. Supervision is performed by healthcare workers or someone nominated by the healthcare worker and the patient for the purpose, and is called a DOT supporter (Corbett *et al.*, 2006; Lewin *et al.*, 2009 and Munro *et al.*, 2007). The DOT strategy has been promoted widely and implemented globally, with success in many countries. Still close to 50% of patients with TB or resistant forms such as XDR-TB do not complete treatment due to various reasons such as erratic drug supply and lack of compliance, which ultimately contributes to prolonged infectiousness, drug resistance, relapse, and death (Garner *et al.*, 2007; Lewin *et al.*, 2009; Munro *et al.*, 2007 and Rubado *et al.*, 2008).

The WHO and United Nation (UN) initiatives for fighting XDR-TB (and other forms of TB) have been a focal point for years. Introduction of the “Stop TB” (and resistant forms)

partnership, aims to halve prevalence and death rates globally by 2015 (Corbett *et al.*, 2007; Hampton, 2004 and Uthman *et al.*, 2009). This seems to be much more of a challenge, especially in Africa and Eastern Europe, than the rest of the world. Preventive interventions such as the WHO '3I's strategy, Intensified case finding, Infection control, and Isoniazid preventive therapy, can offer benefits in the fight against TB (or other forms) with a more focused approach to improving early diagnosis or detection of TB (or other forms), and better disease management to eliminate further infections (WHO, 2008; Reid *et al.*, 2006 and Uthman *et al.*, 2009).

1.1.3 Tuberculosis, Multi-Drug Resistant, Extreme Drug Resistant Tuberculosis and Human Immunodeficiency Virus/Acquired Immunity Deficiency Syndrome

The leading cause of death among HIV/AIDS infected patients in the developing world is TB. An estimated 13% of the 1.5 million TB deaths in 2006 were attributed to HIV/AIDS infection, but in the African region this proportion has been much higher (Wise, 2006).

Numerous medical reports have indicated that HIV/AIDS fuels TB and later XDR-TB (Suchindran *et al.*, 2009; Wilkinson & Davies, 1997 and Wise, 2006). Once someone is infected with TB there is a 5-10% lifetime risk of developing the disease again, but in a person with HIV/AIDS the risk is 5-15% a year (Wise, 2006). Immune suppression in HIV/AIDS infected patients increases the risk of reactivation of latent TB infection and rapid progression to active TB disease. The HIV/AIDS and XDR-TB link is undoubtedly a reality.

Although antiretroviral therapy (ART) can substantially reduce the incidence of TB by 70-90%, recent studies have shown that most children and adults with HIV/AIDS continue to have an elevated risk of contracting TB despite immune reconstitution (Anonymous, 1999). As the HIV/AIDS epidemic increases so does the incidence of TB because of the rapid and widespread dissemination amongst the infected populations. This is due to the increased risk of reactivation in HIV/AIDS patients (Frieden, 2002; Garrait, 1997 and Havlir & Barnes, 1999). As damage to the immune system worsens, people with HIV/AIDS are more likely to develop extra-pulmonary TB.

However, a more recent study has suggested that a high viral load after a TB event may be due to pre-existing high viral load rather than tuberculosis itself (Day *et al.*, 2004 and Goletti *et al*., 1996). Viral load may remain elevated if the tuberculosis is not successfully treated, or may remain elevated in some people despite successful treatment. Africa has experienced 31-38% of TB cases that were due to the HIV/AIDS epidemic (Corbett *et al.*, 2006 and Corbett *et al.*, 2007). Co-infection always poses a challenge to clinicians as

initiation of ART and or termination of TB treatment is not clearly outlined in many countries.

The WHO 2002 guidelines suggested starting antiretroviral drugs within 2 months of tuberculosis treatment, (for extra-pulmonary tuberculosis or other manifestations of severe immunosuppression) in patients with a CD4 count of 200 cells/ µL or less (Havlir *et al.*, 2008 and Lawn *et al.*, 2006). For patients with CD4 counts less than 50 cells/ µL, treatment initiation is advised within 2 weeks.

In a study undertaken by Lawn *et al*. (2006), it was found that earlier initiation of ART may reduce the burden of TB as late initiation of ART was associated with a major burden of TB in the ART programme. In this study, TB reduced survival but did not impair immunovirological outcomes. Therefore, reductions in TB incidence during ART were dependent on CD4 cell count, however, after 3 years of treatment, rates were still 5-10 fold higher than among the uninfected people (Faustini *et al.*, 2006; Havlir *et al.*, 2008; Mitnick *et al.*, 2008; Resch *et al.*, 2006; Suarez *et al.*, 2002 and Suchindran *et al.*, 2009).

Corbett *et al*. (2006) also suggested an early start combined with tuberculosis preventive treatment to contain disease incidence and reduce mortality. The challenge however is that patients who start antiretroviral drugs early in their tuberculosis treatment can be predisposed to immune reconstitution inflammatory syndrome, which is frequent, has symptoms overlapping with worsening tuberculosis and drug reactions, and can be life threatening. It is always advisable for clinicians to consider WHO guidelines for a more systematic approach.

Even though numerous medical reports have outlined the possibilities of linkage between TB (MDR-TB) and HIV/AIDS with each condition responsible for an increase in mortality from the other disease, the relationship is not entirely understood. Difference in opinion from Suchindra *et al.* 2009, studies conducted at various geographic locations, concluded that overall association between resistant forms of TB, MDR-TB, XDR-TB and HIV/AIDS could not be demonstrated. However, results suggested that HIV/AIDS infection is associated with primary MDR-TB and XDR-TB. These reports indicate an association of diseases but not entirely a link with a causality effect (Lawn *et al*, 2002).

It will take some time and further multicentre studies to better understand the association of these two lethal infectious diseases of our generation, although effort and focus are needed to be geared towards controlling the spread of HIV/AIDS and TB (resistant forms: MDR/XDR-TB) diseases in the world.

1.2 SOUTH AFRICAN PERSPECTIVE ON TUBERCULOSIS

South Africa, a home to over 50 million people (Lehohla, 2011), has one of the leading economies on the African continent and is seen as the light of this mother land.

After 18 years of democratic dispensation with improved economic achievements and political stability, SA's public healthcare system is faced with difficulties as is the case in the rest of Africa. TB and HIV/AIDS are among the biggest challenges this country is struggling with.

The introduction of Bacille Calmette-Guerin (BCG), an attenuated strain of *Mycobacterium bovis* introduced as a TB vaccine in the 1920s, was quickly embraced in many areas of the world. Early observational and controlled trials in places such as India and Africa, confirmed the initial claims of efficacy, particularly for meningitis and miliary disease in high-prevalence areas (Cummings, 2007). Through such trials WHO advised countries to incorporate BCG vaccination in their national programs. Though such steps were taken many decades ago the challenges of dealing with TB (resistant forms) in SA still seem fresh, with the HIV/AIDS epidemic compounding the problem. The limitation of BCG is still a failure to protect against adult pulmonary TB, primarily due to the fact that BCG-mediated immunity can only last for 10-15 years where in such cases antimicrobials are an option (Mu *et al.*, 2009). The SA TB treatment (*Annexure 3*) guideline was designed by the WHO and standardised worldwide. *Annexure 1 & 2* guidelines were formulated from successful clinical MDR-and XDR-TB cases based on the latest available information and as seen to be useful in controlling and treating resistant strains in SA, primarily KGH. The world has come to learn from KGH experience in treating XDR-TB cases (Wright *et al.*, 2006).

In 2003, 50% of TB cases and 59% of TB deaths were linked to HIV/AIDS. The number of people co-infected with HIV/AIDS and TB was estimated to be 2 million, which was 8.3% of the adult population of SA (Corbett *et al.*, 2003). The emergence of resistant forms of TB and co-infections with HIV/AIDS, among other opportunistic infections, resulted in the additional burden on limited healthcare resources.

Costs of public medical care continue to escalate annually, with monies spent towards infrastructure upgrades, through the National Department of Health's Revitalisation Plan. The pharmaceutical expenditure is regarded as the second highest expense in SA, after healthcare workers' remuneration in the health budget. Continuous retreatment of TB cases exacerbates the overstretched budget.

The Health Ministry reported in 2006 that the cost for treating a patient with ordinary TB was around R 400.00 per month, and costs escalated if patients defaulted on treatment and developed a MDR-TB with cost of treatment increasing to R 24,000.00 per month including hospitalisation and more expensive drugs (SA DoH, 2006).

1.3 REGIONAL ELEMENT, KWAZULU-NATAL PERSPECTIVE ON TUBERCULOSIS

In 2005, the medical team at the Church of Scotland Hospital (CoSH) in KwaZulu-Natal (KZN), a feeder hospital to KGH, noticed that many patients with TB were not responding to treatment for multi-drug resistant TB (SA DoH, 2006). The Department of Health (DoH) then requested the University of KwaZulu-Natal to investigate the matter. Through that study in a one-year period, 53 patients were diagnosed to have XDR-TB. Fifty-two of these patients died, most within 25 days. Of the 53 patients, 44 had tested for HIV and were found to be HIV-positive. These patients were receiving antiretroviral and responding well to HIV/AIDS-related treatment, but the 52 patients died of XDR-TB (Havlir *et al.*, 2008 and Wise, 2006).

KGH is a regional graded hospital in KZN, situated in Springfield Ward 25 of the eThekwini (Durban) district. It was established in 1939 as a 139 bed hospital to care for TB patients, and today has increased to a 1,291 bed facility with services expanded to include psychiatry, dental, thoracic and orthopedic care. Today it caters for a population of about 9 million TB, MDR-TB and XDR-TB patients.

This research intends to quantify the cost of caring for an XDR-TB patient at KGH. A comprehensive analysis of patient managed care including direct medical and non-medical costs will be considered to attach a monetary value to patient care.

CHAPTER 2

2. AIM AND OBJECTIVE

The aim of the study was to establish:

- The cost implication of treating an XDR-TB patient in a public health facility. The cost incurred will be reported in a daily rate (PDE) and monthly rate (PDE 30 day).

The objective of the study was to establish:

- The PDE cost utilising the formula as stated by the Health System Trust (2009), where a distinction of inpatients, out-patients and day patients has been made. Day patients are patients that are admitted for a day and assigned a bed, but get discharged before midnight on the same admission day. In common practice these patients are regarded as out-patients, but the PDE formula differentiates them to allow for proper cost calculations, assigned to the bed occupancy.

- The direct (medical and non-medical) costs associated with treating an XDR-TB patient in KGH, for inpatient and out-patients, (though not advised to have patients treated from home but allowed due to limited healthcare resources).

- The investigation will seek to compare costs of XDR-TB with treatment length, stay in hospital and out-patient days.

- The investigation will also include the assessment of distribution of the following parameters or profile within the study sample: gender; treatment length for both inpatients and as out-patient; HIV/AIDS status; medical tests conducted; outcome groups; healthcare worker and hospital patient distribution.

XDR-TB occurs as a result of continuous resistance of TB to drugs, and it happens that there's a cross link between TB, MDR- and XDR, hence continuous reference to all three strains.

CHAPTER 3

3. METHODS

3.1 STUDY DESIGN

The study design is a retrospective data analysis, investigating monetary costs incurred by KGH in treating XDR-TB patients. This is limited to patients that have been on treatment prior to commencement of the field work, and will include patients on treatment from January 2002 to December 2007 (as the study field work was initiated in 2008). During the process, the inclusion criteria have been religiously adhered to.

Throughout the research report write up, all three forms of TB will be referred to as there is in some cases a narrow distinction of what form of disease a patient had until laboratory results confirmation of normal TB, MDR-TB, or even XDR-TB. However, cases included in the study had been confirmed to have XDR-TB.

The initial outline on study design had incorporated sample randomisation, but due to limited sample size with 156 credible patient records as per inclusion criteria, the data was included as the sample, and the code referencing maintained (*Appendix 1*), for confidentiality.

Data collection tool used (*Appendix 2*) included all key elements of direct (medical and non-medical) costs. Data from patient records of XDR-TB were kept on an electronic data base using the Windows Access Version 2007 software. The data was extracted and populated onto a Windows Excel Version 2007 document for analysis and proper record keeping.

Confidentiality and consent forms (*Appendix 4*) were adhered to throughout the study. Inclusion and exclusion criteria were also drafted to aid in the selection of patient's records. The criteria were strictly adhered to.

3.2 STUDY SAMPLE

Patient records from 1 January 2002 to 31 December 2007 were entered into the database once confirmed to having met the inclusion criteria. The sample size calculation was done on *Epi-Info* version 3.4.1, and indicated a minimum size as ***n*** value of 100 for statistical significant data. We were able to access 156 suitable patient records from the site.

The following criteria were adhered to when sourcing patient records:

1. Adult patients diagnosed with XDR-TB (≥ 18 years)
2. Patients who were on treatment, terminated or completed, during the specified period of XDR-TB investigation
3. XDR-TB inpatients and out-patients
4. Discharged XDR-TB patients, or transferred to other hospitals
5. Deceased XDR-TB patients who were administered XDR-TB treatment
6. Patients that were diagnosed with XDR-TB between 1 January 2002 to 31 December 2007 period, and were either on treatment or on monitoring/surveillance
7. Patients on XDR-TB treatment, and monitored for over 3 months consecutively (adherence/compliance criteria)
8. Sero-positive and negative patients diagnosed with XDR-TB, on active XDR-TB treatment, or on monitoring/surveillance
9. Patients on XDR-TB treatment, with or without an additional treatment program

Confidentiality was maintained throughout the study, and all parties involved adhered to it.

The inclusion criteria included data from adult's records of XDR-TB diagnosed from a 6 year period to allow sufficient sample size. The HIV status was not excluded from the list.

Patient's compliance was considered to allow for a credible sample where treatment was considered paramount.

Exclusion criteria were also considered to improve on the quality of data available. This included the following:

1. Patients that were already on active XDR-TB treatment at the time of study
2. Patients who were newly diagnosed after commencement of the study
3. Patients younger than 18 years
4. Patients on XDR-TB for less than 3 months consecutively

The exclusion criteria, excluded data from newly diagnosed prospective adult's records, as data collection was initiated in November 2008. Also patients younger than 18 years were excluded based on the study method to include adult patient records only. Patients' compliance was considered to allow for credible sample where treatment was considered paramount. Inconsistencies and interruptions of treatment from patient data were excluded.

XDR-TB was made known to the public in 2006, though cases in KGH have been seen as early as 2001 and initial treatment programs were experimental. The recommended treatment cycle (*Annexure 1-3*) of 6 months for XDR-TB was administered in all cases.

3.3 DATA COLLECTION

KGH was elected to be the study site because it serves as a referral institution and a coordination centre for TB/MDR/XDR-TB treatment in the KZN Province, where CoSH - the first hospital to have the first case of XDR-TB made public, falls within its boundary.

KGH as the study site is a 500 bed facility (and at the time was being upgraded) in the Durban district which caters predominantly for TB patients in the KwaZulu-Natal province, and a number of districts in the northern part of the Eastern Cape province of South Africa. The facility has extended services to include psychiatry and a surgical (thoracic & spinal) unit.

The study sample (or patients records size) was selected based on the inclusion criteria. In total, during the time of data collection at the study sites only 320 patient records could be accessed. The timing of data collection at the State facility was affected by the burden of the disease in the area, at that time, hence the sample size limitations. The 156 patient records out of 320 were eligible to be utilised in the study. The statistician when consulted recommended a minimum of 100 patient records, to offer statistically sound results.

In the results discussion section classification of patient records will be made to indicate outcomes determined based on the treatment period of 12 months when patients were put on treatment. This practice of 12 months outcome observation is common in KGH as it has been used as a determinate of progress in the first 12 months of treatment. The assumption is that the outcome gives an indication of the possibility of the treatment course/path, either in a positive or negative light.

Patient records were investigated for parameters that included information outlined below, but not limited to:

- **Participant Hospital Number**

  The observation offered confidentiality on patient records. The study included this element to protect patient's confidentiality.

- **Gender**

  The observation offered the investigation of statistical comparisons with the opposite gender, and the other elements of the study to draw conclusions from. Information on gender offered insight on the distribution percentage of the gender in the study sample that was affected.

- **Date of Admission**

  The observation offered the investigation statistical comparisons with the other patients' records, and other elements of the study to draw conclusions from. Information on date of admission from patients' records offered insight on the prevalence of XDR-TB in years under study; patient response from treatment versus hospitalisation.

- **Date of Discharge**

  The observation offered the investigation statistical comparisons with the other patients' records, and other elements of the study to draw conclusions from. Information on date of discharge from patients' records offered insight on hospitalisation days.

- **Date of Start of Treatment**

  The observation offered the investigation statistical comparisons with the other patients' records, and other elements of the study to draw conclusions from. Information on date of start of treatment from patients' records offered insight on treatment length - used with date of completion of treatment.

- **Date of Completion of Treatment**

  The observation offered the investigation statistical comparisons with the other patients' records, and other elements of the study to draw conclusions from. Information on date of completion of treatment from patients' records offered insight on treatment length - used with date of start of treatment.

- **Out-Patient Days on Treatment**

  The observation offered the investigation statistical comparisons with the other patients' records, and other elements of the study to draw conclusions from. Information on out-patient days on treatment of patients' records offered insight on number of days on treatment out of hospital.

- **HIV/AIDS Status** (where applicable)

  The observation offered the investigation statistical comparisons with the other patients' records, and other elements of the study to draw conclusions from. Information on

HIV/AIDS status from patients' records offered insight on HIV/AIDS prevalence from the study sample; link between HIV/AIDS and TB and treatment success within the HIV/AIDS positive group.

- **Medical test and care conducted/offered**

  The observation offered the investigation statistical comparisons with the other patients' records, and other elements of the study to draw conclusions from. Information on medical test and care conducted/offered from patients' records offered insight on other costs incurred whilst on XDR-TB treatment.

3.4 COST CALCULATION

The quantification of costs considered for the study was split into direct (medical and non-medical) costs, as outlined in figure 3.4.1, below.

This schematic diagram indicates the various cost components that could be analysed for any study. **For the purpose of this project only the direct medical and non-medical costs were considered**.

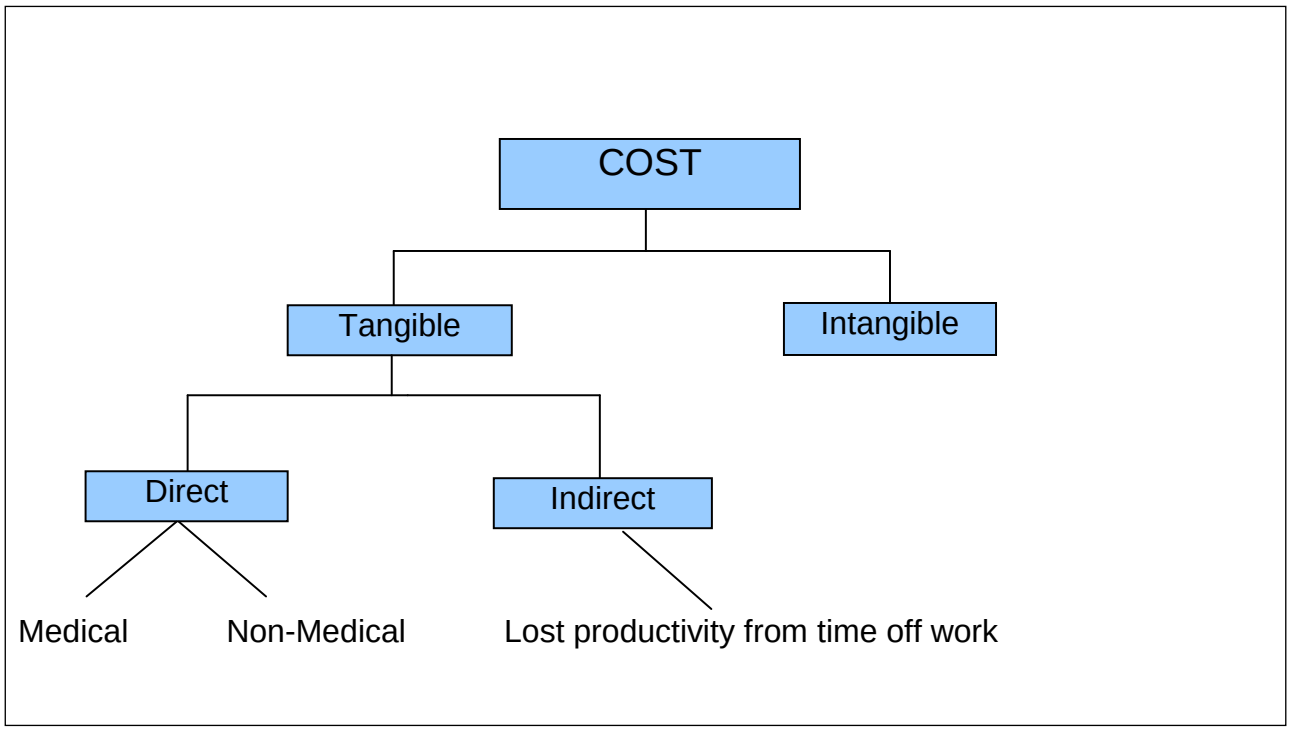


Figure 3.4.1: Monetary Value Analysis (Maynard *et al.*, 1992)

The other cost element considered was patient day equivalence (PDE) which is the indicator that measures how the resources available to the hospital are being spent, and is a marker of the efficiency of the hospital as a whole.

PDE cost encompassed the total daily costs to the hospital of caring for a patient (Thomas *et al.*, 2007). PDE was useful as a tool to summarize the average patient daily treatment expenditure. It is a composite process indicator in that it links financial data with service-related data from the hospital admissions and outpatients.

The formula used by public sector hospitals to estimate the PDE cost, using data from the financial year's expenditure, was as follows:

$$\textbf{PDE Cost} = \frac{\textbf{Total Hospital Expenditure}}{\textbf{(Average number of inpatients) + (0.5 X Average number of day patients) + (Average number of out-patients X 0.33)}}$$

(*Equation 3.1)*

The PDE as a measure of the volume of patients seen in hospital also accounts for all the patients that do not spend a full day (from midnight to midnight) at the hospital, as these day patients, out-patients, and emergency room visit patients add to the workload of the hospital calculated in the equivalent number of 24-hour patients (HST, 2009).

The formula included annual direct costs incurred by the hospital, the cost of personnel (doctors, nurses, and other healthcare workers), and non-medical costs. It also incorporated annual inpatients numbers, weighted annual out-patients' contributions and day-case contributions; and allowed for cost comparisons between hospitals. The primary results of XDR-TB costs will be based on PDE calculations and results thereof as in Table 4.2.1.

The fieldwork site visit included departments involved in treating XDR-TB patients to ascertain the extent of work involved, and costs incurred in the process. These included but were not limited to pharmacy, medical wards, laboratory, X-ray, kitchen, medical stores and audiology department due to side effects profile of antiretroviral drugs causing hearing loss. The hospital finance department was however not forth coming with information on costs of administration, hospitalisation and personnel, as they deemed information to be confidential. Although this information was sourced, it's secondary to the PDE calculations as the accurate measure of treatment cost in the public health facility.

Investigation on costs assessments at the departments resulted in the cost as tabled, but not limited to the list below:

Table 3.4.1: List of Direct Cost Breakdown

Direct Cost	Comment
i) Medical	
Diagnostic test (X-ray)	R 220.00 per test
Admission Fees (Administrative fee)	PDE determined
Diagnostic test (Audiology tests)	R 25.00 per test
Medications cost (Drugs)	See *Appendix 5*
Diagnostic Bed Side Tests: Blood Glucose, Temperature Test, Blood Pressure	PDE determined
Other tests costs	See Table 4.11.2
Hospitalisation fee/day	PDE determined
In Hospital diet/nutrition	R 25.00 per day
Laboratory tests (Blood, Urine)	R 22.00 per test
Microbiological tests (Sputum Culture)	R 45.00 per test
Pharmacy time, and counseling	PDE determined
Consultation costs	
Nursing time and counseling	
Allied Services rendered: Physiotherapy; Occupational therapist and Social Worker	
ii) Non-Medical	
Telephone calls	No telephone call allowed except in emergency situations, and these were not monitored
Special diet (lunch packs)/allowance	No special lunch
Child care costs	none
Samples Courier	none
Transportation	Hospital does not transport any patients except within the hospital. Patients referred to King George for admission or monthly visits are transported by Elective planned transport or Emergency Medical Rescue Services (EMRS). KZN province has a cost but no direct cost to hospital. Patient cost per trip within the 100km radius of hospital is R 15.50

3.5 DATA ANALYSIS

The calculations on costs involved in XDR-TB, was through the use of a PDE cost calculation formula to indicate a general economics understanding on an individual cost for treatment by a hospital like KGH. In this case monthly costs of R 77,404.00 in 2002 and R 144,221.00 in 2007 were noted, as inflationary-adjusted to 2012 cost (as per results produced in Table 4.2.1).

Table 4.2.1 indicated the parameters that were involved with cost calculation, as inflation percentages were utilised to indicate present values. The hospital data was collected and analysed using *Epi-Info* version 3.4.1 software, and Microsoft Access Version 2007.

Descriptive statistics of continuous (numerical) variables were included as measures of central tendency (mean and median) and measures of variability (standard deviation). For categorical data, the descriptive results included frequency (number) distribution tables and bar charts. The total cost was estimated using the information gathered from personal details, medical history, laboratory results, treatment regimen and other costs incurred (medical and non-medical costs). Categorical variables were analysed using the Pearson's chi-square test (and the Fisher's Exact Test, where appropriate).

Linear regression was used to find the relationships between the costs and other explanatory variables, in the univariate analysis. The regression table was analysed to determine variability of data and the F-distribution, as a measure of significance on the model. The coefficient of determination (R^2) was used to measure the variability in the Y explained by an X variable. Statistical significance was ascertained at the five percent (5%) level of significance (for *p* values less that 0.05). The data was analysed using *Epi-Info* version 3.4.1, Microsoft Excel Version 2007 and STATA 10.0.

CHAPTER 4

4. RESULTS

In 2002 financial year, it cost an average of R 45,060.00 to treat an XDR-TB patient in hospital for 30 days. Over the years from 2002 to 2007, there has been an increased shift in inpatients and day patients numbers, attributable to two reasons: (a) the increase in surveillance and detection of XDR-TB by medical practitioners; (b) the availability of beds within the facility to accommodate the XDR-TB patients, as the less severe forms of TB resulted in early discharge as opposed to the latter. In 2007 PDE costs had escalated to R 104,430.00 per patient, with treatment success rate still being a challenge for XDR-TB.

4.1 INCREASES IN PDE COSTS PER YEAR

The XDR-TB PDE expenditure of patients in 2002 was R 1,502.00, and calculations were based on information in table 4.2.1 as sourced from KGH. The initial years of XDR-TB detection and treatment were based on a few numbers of patients, and in later years the picture of costs and patient numbers had begun to increase, as healthcare providers became vigilant of the disease.

4.2 INFLATION INCREASE ON PDE

The impact of inflation on PDE's was calculated from data obtained from STATS SA (sourced through http://www.statssa.gov.za/keyindicators/CPI/CPIHistory.pdf); so that the increase on PDE in real terms could be established. The consumer price index (CPI) averages as obtained through STATS SA, were also used to extrapolate 2008 data till 2012 for XDR-TB PDE costs. .

The concept of net present values (NPV) as learned though accounting principles from Mills & Print (2006) brings about the knowledge to compound present values into future values.

The present values as stated in 30 days of XDR-TB was calculated and included inflationary figure to depict real time values of 2012, utilizing the equation 4.1 as outlined below.

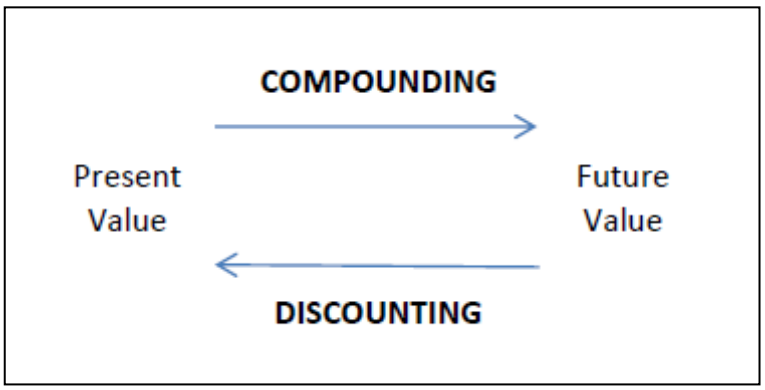


Figure 4.2.1: Compounding and discounting cash flow principles (Mills & Print, 2006)

FV= PV (1 + rt) *(Equation 4.1)*

FV: is the Future Value
PV: is the Present Value
(1+rt): is the rate of interest in years

Table 4.2.1 indicates the calculated future values in real time (2012), and was obtained by compounding each year's values by the rate of interest on an annual basis to achieve the 2012 values. The example below indicates the calculations:

TAKING 2002 VALUE TO 2012 REAL TIME

FV (2003) = 45,060.00 (1 + 5.8%) = 47,673.00	STEP 1
FV (2004) = 47,673.00 (1 + 1.4%) = 48,341.00	STEP 2
FV (2005) = 48,341.00 (1 + 3.4%) = 49,984.00	STEP 3
FV (2006) = 49,984.00 (1 + 4.6%) = 52,284.00	STEP 4
FV (2007) = 52,284.00 (1 + 7.2%) = 56,048.00	STEP 5
FV (2008) = 56,048.00 (1 + 11.5%) = 62,494.00	STEP 6
FV (2009) = 62,494.00 (1 + 7.1%) = 66,931.00	STEP 7
FV (2010) = 66,931.00 (1 + 4.3%) = 69,809.00	STEP 8
FV (2011) = 69,809.00 (1 + 5.0%) = 73,299.00	STEP 9
FV (2012) = 73,299.00 (1 + 5.6%) = 77,404.00	STEP 10

The compounding calculation made in each year to the 2012 period, to achieve the real time value.

EXTRAPOLATION OF PDE COST FROM 2008 TO 2012

The PDE value sourced were only stated till 2007, and the exercise to extrapolate from 2007 on an annual basis till 2012 was based on the CPI rate increase. The method of extrapolation is similar to the FV calculations as stated above.

Example:

PDE (2008): PDE (2007) (1+ rt)
= 3,124 (1+11.44%)
= 3,481.00

Table 4.2.1: XDR-TB PDE Costs with Inflation

Years	Total XDR TB Expenditure	Average number of XDR-TB inpatients	Average number of XDR-TB day patients	Average number of XDR-TB outpatients	XDR-TB PDE Costs (Rand)	XDR-TB Costs (Rand) for 30 Days	Total inflationary effect for the period 2003 to 2012	XDR-TB Costs (Rand) for 30 Days in 2012 Prices
2002	297,386	9 ±2.49	40 ±5.98	512 ±10.51	1,502 ±233.53	45,060	9.10%	77,404
2003	358,923	11 ±1.71	52 ±3.62	536 ±13.06	1,678 ±241.91	50,340	5.80%	81,733
2004	633,248	36 ±5.06	59 ±6.51	625 ±4.86	2,330 ±276.31	69,900	1.40%	111,925
2005	998,900	83 ±3.91	102 ±6.84	729 ±26.33	2,667 ±304.80	80,010	3.40%	123,900
2006	1,472,500	168 ±5.74	148 ±12.14	695 ±13.08	3,124 ±257.08	93,720	4.60%	138,749
2007	1,672,000	139 ±11.62	166 ±5.06	783 ±15.05	3,481 ±301.84	104,430	7.20%	144,221
2008					3,881	116,439	11.50%	144,221
2009					4,157	124,707	7.10%	144,221
2010					4,336	130,069	4.30%	144,221
2011					4,552	136,572	5.00%	144,221
2012					4,807	144,221	5.60%	144,221

4.3 TREATMENT TIME AND XDR-TB PDE

The results on regression indicate that XDR-TB PDE costs are directly proportional to the increase in years as a time period, which is as expected.

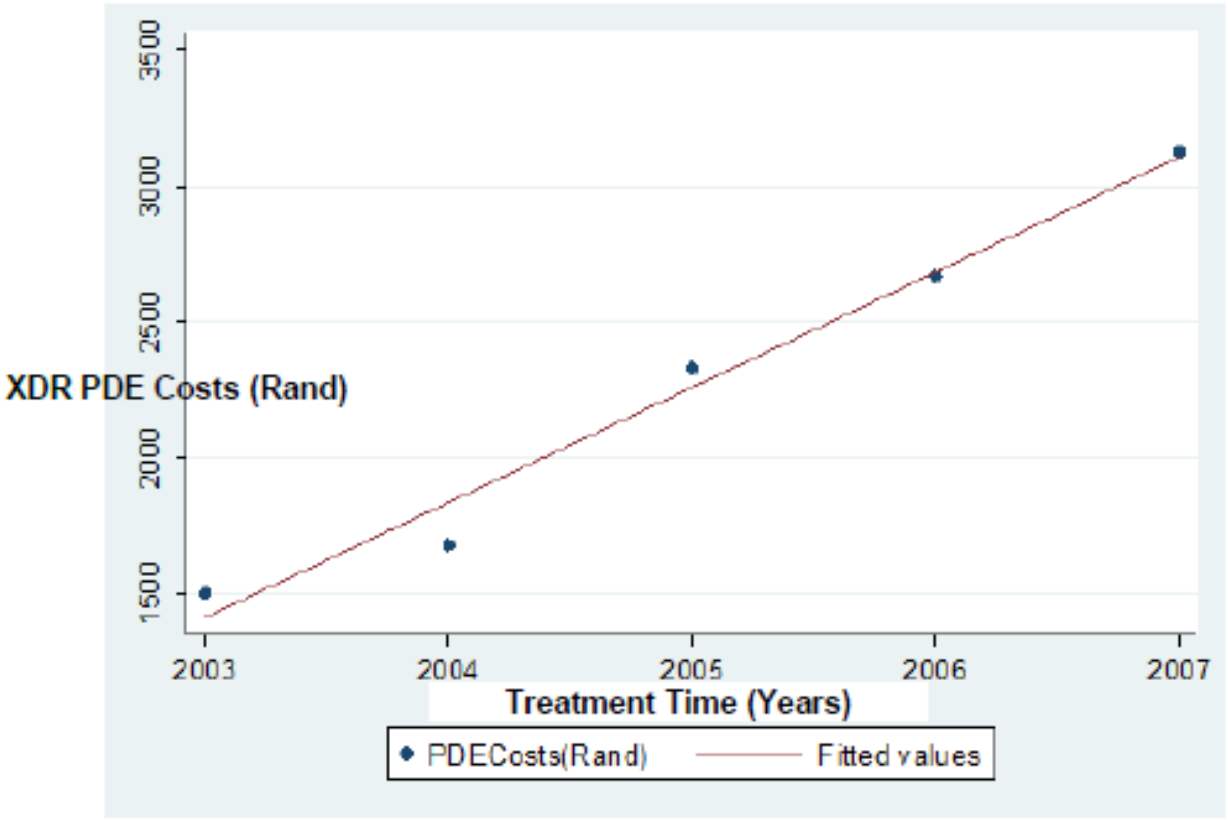
Table 4.3.1: Regression on treatment time (Years) and XDR-TB PDE costs (Rand)

PDE Cost (Rand)	Coef	Std. Err	t	P>|t|	[95% Conf. Interval]	
Year	423.2	35.67763	11.86	0.001	309.6579	536.7421
Constant	-846,255.6	71,533.67	-11.83	0.001	-1,073,908	-618,603.5

Number of patients = 156
F (1, 3) = 140.70
Probability > F = 0.0013
R-squared = 0.9791
Adj R-squared = 0.9722

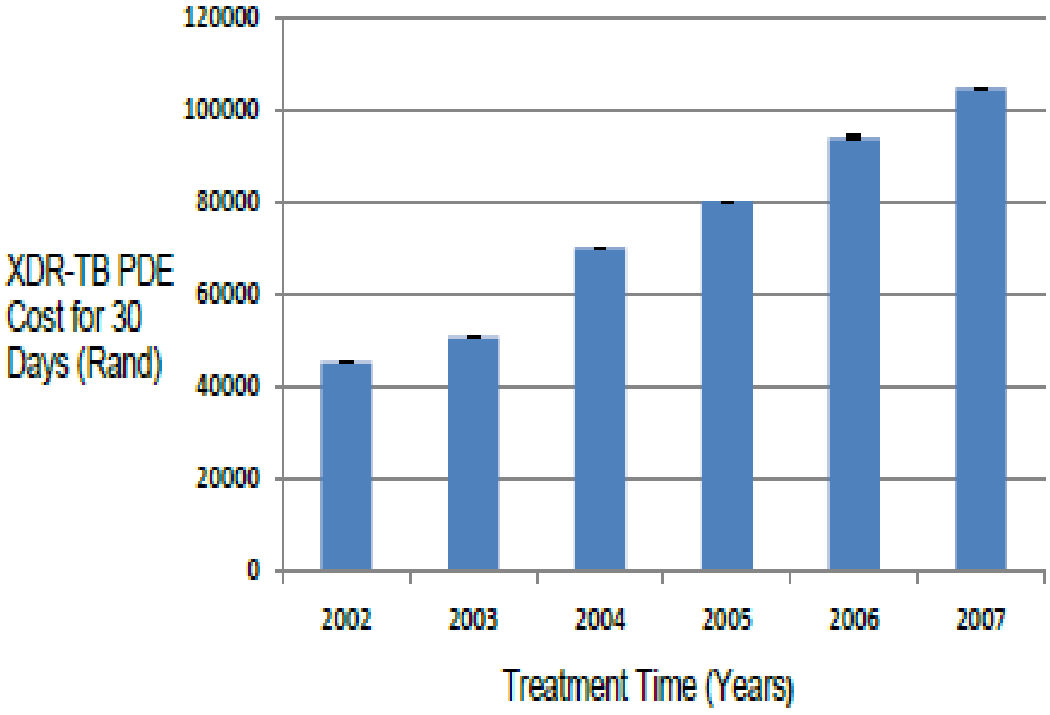
XDR-TB PDE cost = 423.20 x year + (-846,255.60)

There is a general cost of R 423.20 that escalates PDE cost annually over the period of six years. The linear relationship between XDR-TB PDE cost as the dependent (outcome) and year as the independent was statistically significant. F (1, 3) = 140.70 with a *p-value* = 0.0013. The coefficient of determination (R^2) shows that 97.91% of the variability in PDE costs can be explained by the years on treatment. The total amount of PDE cost increased at the rate of R 423.20 for each year patients are put on XDR-TB treatment.



Graph 4.3.1: Treatment Time (Years) vs. XDR PDE Costs (Rand)

Graph 4.3.1 depicts the linear relationship as fitted, to indicate that PDE costs are directly proportional to the increase in years as a time period. The XDR-TB PDE costs in relation to spotted values in time (years) indicates an increase in cost of treatment with the nature of drugs utilised to combat the condition over months and years on treatment. The increase in PDE in each year also has to do with a change in patient days, out-patient and inpatient distribution, and increased numbers of diagnosed patients put on treatment.



Graph 4.3.2: Treatment Time (Years) vs. XDR-TB PDE Cost (Rand) for 30 Days

The XDR-TB treatment cost was calculted in real time value as of 2012 where inflationary impact has been accounted for, for a period of a month (30 days) treatment. Costs of the disease increased over the years and there are various reasons for that, and on a face value one can expect it to be due to an increase in annual medication and staff costs, but there is also the fact that as a new disease, XDR-TB had started to be detected by healthcare professionals during the screening phase and the community became aware of the condition. With TB being a notifiable disease this also translated to XDR-TB being reported to the authorities and the country became aware of the condition as well. In general the costs escalation were attributable to increased numbers of patients and treatment time required to treat an XDR-TB sufferer.

4.4 XDR-TB TOTAL TREATMENT LENGTH; LENGTH OF STAY IN HOSPITAL AND OUT-PATIENT DAYS

Table 4.4.1: XDR-TB Total Treatment Length (Days); Length of Stay in Hospital (Days) and Out-patient days (Days)

Variable	Average number of days	Std. Dev.	Min	Max
Length of stay in hospital	78.4808	70.1574	0	251
Out-patient days	105.436	107.846	0	358
XDR TB total treatment	180.917	108.655	0	358

Comments:

The standard treatment guideline (*Annexure 3*) of TB requires six months of chronic treatment, and recommended for patients to be hospitalised for both MDR-and XDR-TB due to the resistant nature of the bacteria, to prevent further infections. Table 4.4.1 depicts average number of days patients spent in hospital, also as out-patients as well as being on XDR-TB treatment based on the study sample. The interest in distinction of days spent as either out-patient or inpatient (stay in hospital) is due to varying costs of the two categories which ultimately impacts on the public hospital expenditure.

The 156 patients observed length of stay in hospital, had an average of 78.48 days; with maximum of 251 days for the longest stay patient. Out-patients days once discharged, had an average of 105.44 days and maximum out-patient days of 358 for a patient. Generally the distribution of patient days as either inpatient or out-patients indicates that when the condition has been controlled patients would be discharged to continue the treatment at home, but we are also aware that only a small proportion of patients were accommodated in hospital as there were limited bed facilities, so it meant that even though the out-patients days are potentially longer based on treatment pattern, but they were also longer due to those patients that were initially meant to be hospitalized as treatment was initiated. These costs difference were incorporated in the PDE calculation as data in table 4.2.1

The XDR-TB treatment days, is a measure of how long patients have been on chronic treatment. This was worked out as the length of stay in hospital on treatment added with out-patient days on treatment. Observations of 156 patients had average days on treatment of 180.92 days; standard deviation of 108.65 days, and maximum days on treatment for a patient was 358.

4.5 LENGTH OF STAY IN HOSPITAL AND TOTAL MEDICAL COSTS

Table 4.5.1: Correlation on Length of Stay in Hospital (Days) and Total Medical Costs (Rand)

	Medical Total	Length of Stay
Total medical cost	1.00	
Length of stay	0.2596	1.000
p-value	0.0011	

Comments:

The XDR-TB PDE calculation indicated a daily cost of hospitalisation, and the correlation (r) of total medical inclusive of drug costs, showed a positive correlation. There is a 0.2596 correlation between medical costs and length of stay in hospital, which is a 26% percent correlation. The statistical significance validity of this correlation is represented by a *p-value* of 0.0011 (statistical significance of $p < 0.05$). Hence we then proceed to do the regression to determine the daily impact (length of stay) to the medical cost.

Table 4.5.2: Regression on Length of Stay in Hospital (Days) and Total Medical Costs (Rand)

Total Medical Cost	Coef	Std. Err	t	P>|t|	[95% Conf. Interval]	
Length of stay in hospital	201.04	60.26	3.34	0.001	81.993	320.0802
Constant	74,681	6,334.4	11.79	< 0.001	62,167.2	87,194.42

Number of patients	=	156
F (1, 154)	=	11.13
Probability > F	=	0.0011
R-squared	=	0.0674
Adj R square	=	0.0613

Total medical cost = 201.04 x Length of stay in hospital + 74,681

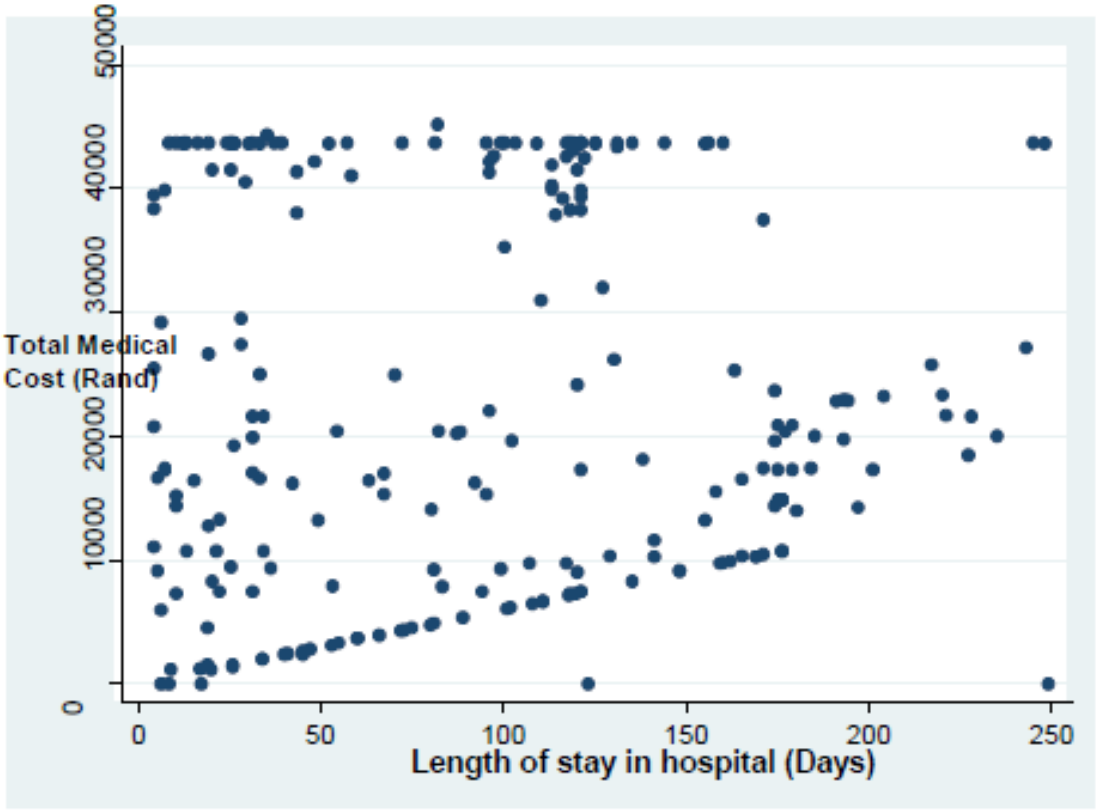
Comments:

The results on regression indicate that medical costs are directly proportional to the increase in the length of stay in hospital as expected. The linear relationship between total medical costs as the dependent (outcome) and length of stay in hospital as the independent was statistically significant. F (1, 154) = 11.13 with a *p-value* = 0.0011. The coefficient of determination (R^2) shows that 6.74% $(0.2596)^2$ of the variability in medical costs can be explained by the length of stay in hospital. The total amount of medical cost increased at the rate of R 201.04 for each day the patient was on XDR-TB treatment and

associated conditions in hospital. The 95% confidence interval was (81.99296 - 320.0802) *p-value* = 0.001, with cost of daily rate ranging between R 81.99 and R 320.08. This meant that patients on a standard drug regimen could easily be calculated on cost to hospital.

Though there was a potential limitation on cost calculation on patients that have only been in hospital for observation with no medical and non-medical costs, hence the out-patient numbers in table 4.2.1 are different to the day patient. The distinction was based on whether the patient was booked in for a day and discharged in the case of a day patient, or was part of an emergency case, or on routine check-up (as outpatient); and cots were able to be allocate as such. Hence XDR-TB PDE is utilised as a useful tool to incorporate such costs as incurred by the hospital.

Associated conditions considered varied based on the patients' state of health, but they were all acute in nature, from analgesics, oral topical to vitamin tablets. *Appendix 5* lists medication cost that determined the total medical cost.



Graph 4.5.1: Length of Stay in Hospital (Days) vs. Total Medical Costs (Rand)

Comments

We can fit a linear pattern to the low costs medical versus days of stay, though the high medical costs are not perfectly linear. The increased cost at admission or early days of

stay in hospital; is an indication of other medical conditions that a patient might be suffering from which is a general picture in most disease states when monitored.

For each day spent in hospital, there is an R 201.03 increase rate in costs. The cost of R 201.03 for the sample size is related to only medication whilst in hospital, as out-patient costs are excluded but incorporated in PDE calculations.

Simply, explained as an increase in length of stay will cause a 0.2596 increase in total medical costs.

The statistical significance validity of correlation is represented by a *p-value* of 0.0011 (Statistical significance of $p < 0.05$).

4.6 LENGTH OF STAY IN HOSPITAL AND TOTAL NON-MEDICAL COSTS

Table 4.6.1: Correlation on Length of Stay in Hospital (Days) and Total Non-Medical Costs (Rand)

	Total non-medical costs	Length of stay
Total non-medical costs	1.000	
Length of stay in hospital	1.000	1.000
p-value	< 0.001	

Comments:

Similarly with medical costs, the non-medical costs such as sundries and dressings will have a positive correlation as an increase in length of stay will cause a direct increase in non-medical costs. There is a 1.00 correlation between non-medical costs and length of stay in hospital, which is a 100% percent correlation. The statistical significance validity of this correlation is represented by a *p-value* < 0.0001. Hence we then proceed to do the regression to determine the daily impact (length of stay) to the non-medical cost.

Table 4.6.2: Regression on Length of Stay in Hospital (Days) and Total Non-Medical Costs (Rand)

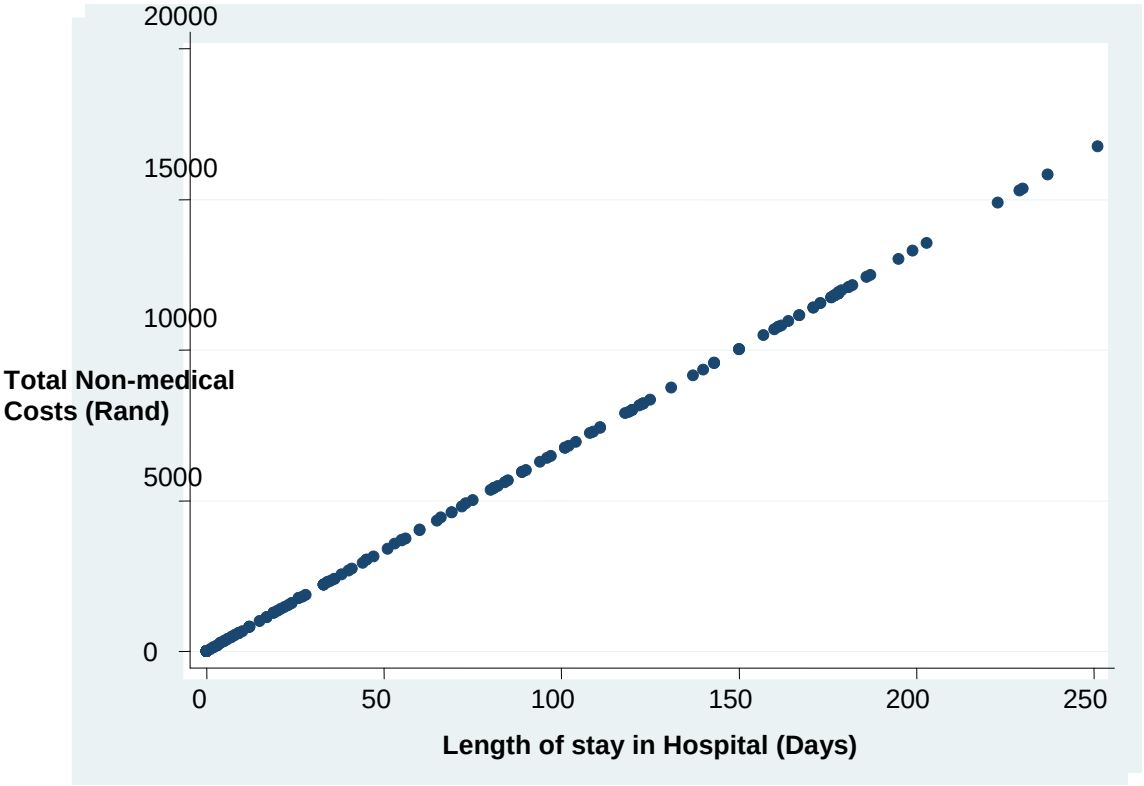
Total non-medical costs	Coef	Std. Err	t	P>|t|	[95% Conf. Interval]	
Length of stay in hospital	66.7653	0.0091994	7,257.57	< 0.001	66.74709	66.78344
Constant	2.62111	0.9670198	2.71	0.007	0.7107724	4.531444

Number of patients	=	156
F (1,154)	=	11.13
Probability > F	=	<0.001
R-squared	=	1.0000
Adj R-squared	=	1.0000

Total non-medical costs = 66.7653 x length of stay in hospital + 2.62111

Comments:

The results of regression indicate that non-medical costs are directly related to the increase in length of stay in hospital. The linear relationship between total non-medical costs as the dependent (outcome) and length of stay in hospital as the independent was statistically significant. F (1, 154) = 11.13 with a *p-value* = <0.001. The total amount of non-medical costs increased at the rate of R 66.77 for each day the patient was on XDR-TB treatment in hospital relayed by coefficient data [P value was 0.000 and the 95% confidence interval (66.74709 - 66.78344)] , with cost of daily rate ranging between R 66.75 and R 66.78.



Graph 4.6.1: Length of Stay in Hospital (Days) vs. Total Non-Medical Costs (Rand)

Comments

The above graph depicts a clear linear correlation between non-medical costs and length of stay in hospital. Nursing care for patient in hospital is standardised by nursing protocol and non-medication costs that are incurred by all patients equally, based on length of stay irrespective of time spent to care for a specific patient.

This is a totally different principle as opposed to motor vehicle industry where labour spent repairing a car will be calculated at an hourly rate. To simplify the daily rate on non-medication cost for the study sample of 156: for each day spent in hospital, there is a R 66.77 increase rate in costs.

Nursing protocol outlined a general utilization method of sundries, dressing and routine sample collections after certain days have lapsed. In general it makes reasonable sense to have a linear relationship between days spent in hospital to increase linearly with non-medication cost incurred.

The statistical significance validity of correlation is represented by a *p-value* of less than 0.0001; (statistical significance of $p < 0.05$).

4.7 XDR-TB TOTAL TREATMENT LENGTH AND TOTAL COSTS

Table 4.7.1: Correlation on XDR-TB Total Treatment Length (Days) and Total Costs (Rand)

	Total costs	Total XDR-TB treatment length
Total costs	1.000	
Total XDR-TB treatment length	0.9967	1.000
p-value	< 0.001	

Comments:

The total cost includes all treatment costs of medical and non-medical costs. The correlation between total cost and XDR-TB total treatment indicates a linear pattern, as increase in XDR-TB total treatment will directly increase costs. There is a 0.997 correlation between total costs and total XDR-TB treatment length, which is a 99.7% percent correlation. The statistical significance validity of this correlation is represented by a *p-value* < 0.001.

Table 4.7.2: Regression on XDR-TB Total Treatment Length (Days) and Total Costs (Rand)

Total cost	Coef	Std. Err	t	P>|t|	[95% Conf. Interval]	
XDR-TB total treatment	511.17	3.355261	152.35	< 0.001	504.5415	517.7981
Constant	3,221.61	707.4825	4.55	< 0.001	1,823.989	4,619.235

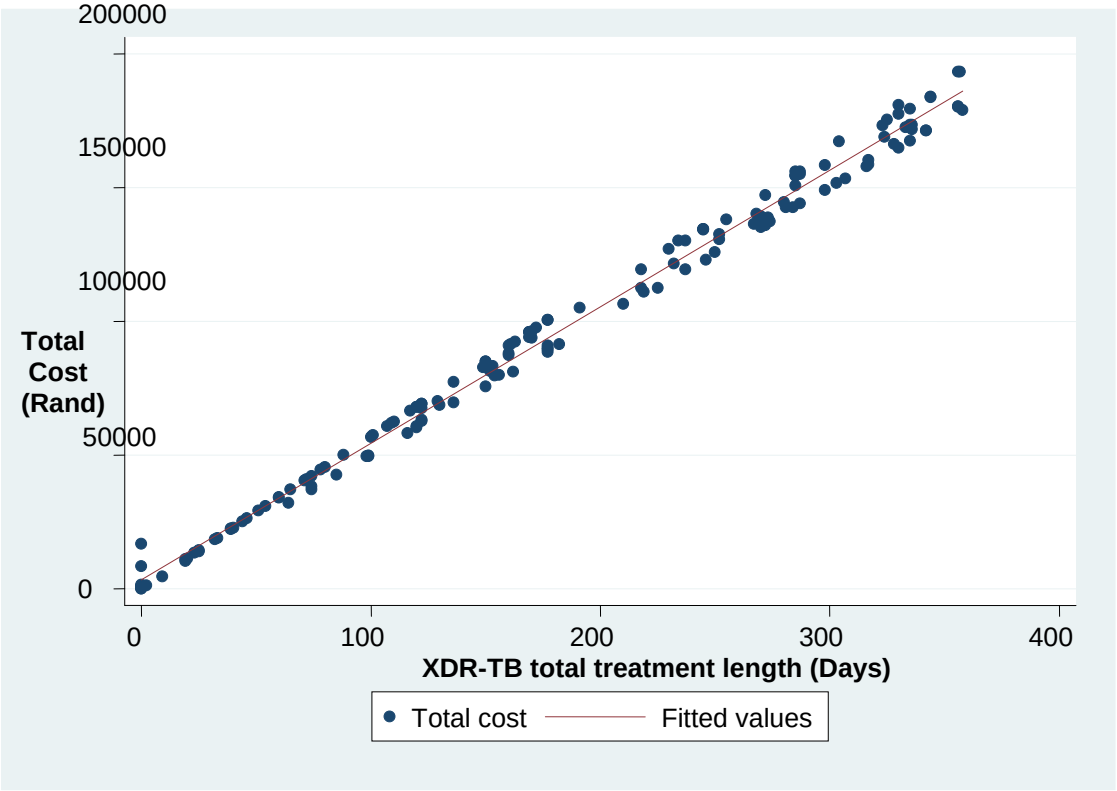
Number of patients	=	156
F (1,154)	=	23,210.14
Probability > F	=	0.0000
R-squared	=	0.9934
Adj R-squared	=	0.9934

Total costs = 511.17 x XDR-TB total treatment length + 3,221.61

Comments:

The results on regression indicate that total cost of both medical and non-medical costs are directly proportional to the increase in the length of stay in the hospital. The linear relationship between total costs as the dependent (outcome) and XDR-TB total treatment length as the independent was statistically significant. F (1, 154) = 23,210.14 with a *p-value* = 0.0000. These costs increased at the rate of R 511.17 for each day the patient was on

XDR-TB treatment and associated conditions in hospital. XDR-TB treatment in hospital relayed by coefficient data [P value was 0.000 and the 95% confidence interval (504.5415 - 517.7981)], with cost of daily rate ranging between R 504.54 and R 517.80.



Graph 4.7.1: XDR-TB Total Treatment Length (Days) vs. Total Costs (Rand)

Comments:

The total treatment length and total cost indicated a linear correlation with each day spent on XDR-TB treatment, there was generally a daily increase rate of R 511.16. The composition of total cost included medical and non-medical, with non-medical cost indicated a linear pattern on cost in relation to treatment days in hospital. It was not surprising to realize that total cost depicts the same pattern. The study sample has had more out-patient treatment days than the inpatient days, and the cost of R 511.16 has composition mostly of hospitalisation compounded with medical costs. Should the inpatient days been more than the outpatient numbers, the picture would have been much worse as in-hospital treatment costs are much more expensive.

The statistical significance validity of correlation is represented by a *p-value* of less than 0.0001; (statistical significance of $p < 0.05$).

4.8 OUT-PATIENT DAYS AND TOTAL MEDICAL COSTS

Table 4.8.1: Correlation on Out-Patient Days (Days) and Total Medical Costs (Rand)

	Total medical costs	Outpatients days
Total medical cost	1.000	
Outpatient days	0.7943	1.000
p-value	< 0.001	

Comments:

The hospitalised patients cost are easily determined as patients are within the institution, whilst out-patients costs are somewhat complex though direct costs come from treatment issued on a monthly basis, and clinical personnel time from pharmacy, doctor's consultation with administration cost at times. Hence the XDR-TB PDE calculation is used as a tool to comprehensively determine such costs for the institution.

The correlation between total medical costs and out-patient days indicates a linear pattern, as increase in out-patient days will directly increase medical costs. There is a 0.7943 correlation between total medical costs and out-patient days, which is a 79.43% percent correlation. The statistical significance validity of this correlation is represented by a *p-value* < 0.001.

Table 4.8.2: Regression on Out-Patient Days (Days) and Total Medical Costs (Rand)

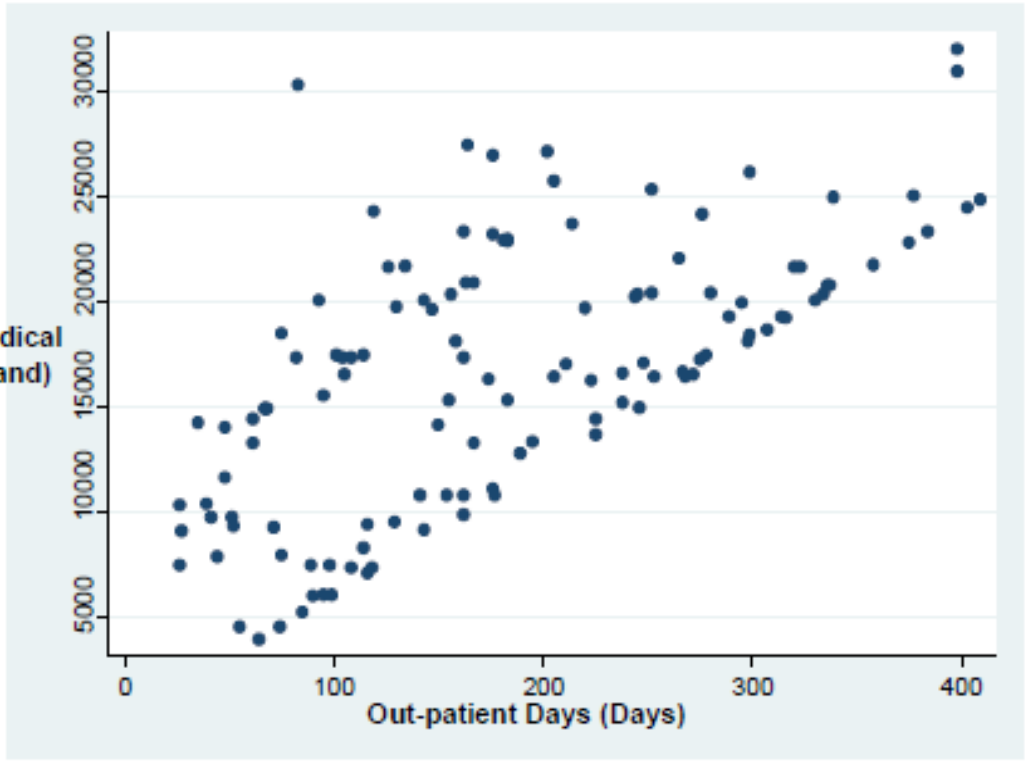
Total costs	Coef	Std. Err	t	P>|t|	[95% Conf. Interval]	
Outpatient	400.13	24.6613	16.23	0	351.412	448.848
Constant	48,270.30	3,713.38	13	0	40,934.6	55,606

Number of patients	=	156
F (1, 154)	=	263.25
Probability > F	=	0.0000
R-squared	=	0.6309
Adj R-squared	=	0.6285

Total costs = 400.13 x Outpatient days + 48,270.3

Comments:

The results on regression indicate that medical costs are directly linked to the increase in the out-patient days on treatment. The linear relationship between total medical costs as the dependent (outcome) and out-patient days as the independent was statistically significant. F (1, 154) = 263.25 with a *p-value* = 0.0000. The total amount of medical cost increased at the rate of R 400.13 for each day the patient was on XDR-TB treatment and associated conditions as out-patient relayed by coefficient data [P value was 0.000 and the 95% confidence interval (351.4117 - 448.8478)], with cost of daily rate ranging between R 351.41 and R 448.85.



Graph 4.8.1: Out-Patient Days (Days) vs. Total Medical Costs (Rand)

Comments:

The above graph represents a 0.7943 correlation between out-patient days and medication costs; with each day spent as an out-patient, there was an increase rate of R 400.13 for medication costs directly related to XDR-TB chronic treatment and associated conditions. The increased cost at consultation or zero out-patient day; is an indication of other medical conditions that a patient might be suffering from; which is a general picture in most disease states when monitored. The PDE calculation data has shown an annual increase on out-patient head count, and medical costs have also increased with more patients getting treated out of hospital together with continuous infections within the communities.

It is not advisable to have XDR-TB patient treated out of hospital but due to limited bed space, the KGH allowed some patients that have low risk of causing further infections to others, also those seen to be responsive to treatment and those that were compliant to treatment, to be treated as out-patients.

The statistical significance validity is represented by a *p-value* of less than 0.0001 (Statistical significance of $p < 0.05$).

4.9 DISTRIBUTION ON MEDICAL AND NON-MEDICAL COSTS

Table 4.9.1: Non-Medical; Medical and Total Costs

Variable	Mean	Std. Dev.	Min	Max
Total non-medical	5,242.41	4,684.08	0	16,757.2
Total medical	90,458.3	54,327.3	0	179,000
Total costs	95,700.7	55,724.9	0	193,388

Comments:

Formulation of direct medical and non-medical costs for the sample size is adequate to have an understanding on total direct cost of treating an XDR-TB patient. The cost of non-medical treatment of the 156 patients had a mean cost of R 5, 242.41; standard deviation of R 4,684.08 and maximum total non-medication of R 16,757.24 for the longest stay in hospital.

The cost of medical treatment of the 156 patients had a mean cost of R 90,458.33; standard deviation of R 54,327.26 and maximum total medication of R 179,000 for the longest stay in hospital, of 251 days.

Total cost of treatment was calculated as the sum of the non-medication and medication costs of both hospitalised and out-patient days. The 156 observations had a mean of R 95,700.74; standard deviations of R 55,724.86 and maximum cost of R 193,387.90 for the patient with the longest treatment days. In summary, generic cost determined without utilizing XDR-TB PDE formula indicates that on average to treat an XDR-TB patient with associated conditions such as acute or pain, and inclusions of cough mixtures and vitamins which are quite common at cost of R 95,700.74 with cost escalating to R 193,387.90 for non-responsive and complicated cases in the period of 2002 - 2007 values.

4.10 DISTRIBUTION ON OUT-PATIENTS

Table 4.10.1: Out-Patients Distribution

Out-patient	Patients	Percentage	Cumulative
False	137	87.82	87.82
True	19	12.18	100
Total	156	100	

Comments:

The standardised management of TB requires that patients be hospitalised especially for the severely affected or with resistant forms of TB.

Table 4.10.1 depicts a comforting picture of less than 13% patients being treated as out-patients, although not advisable to have an XDR-TB sufferer treated out of hospital. Since public health facilities have limited resources to accommodate all MDR- and XDR-TB patients, and it gets difficult to get space as most of the admitted patients stay in hospital for a minimum of two months in most cases.

The study sample had only 12.18% (19 patients) as out-patients and the 137 patients (87.82%) were all hospitalised.

4.11 DISTRIBUTION ON INVESTIGATIVE TESTS

Calculations of various tests conducted over a 6 year period (2002 - 2007) of analysis with each patient record of a 365 days cycle for the study sample, resulted in the tabulated data below.

Table 4.11.1: Tests of laboratory procedures on Laboratory Cultures; Sputum Sample; Audiology; Urine and Electrolytes; X-ray; Meals consumed and Urine Dip Sticks

Variable	Average number of tests patients	Std. Dev.	Min	Max	Cost/Test (Rand)*
Lab cultures	5.641	5.0302	0	18	120*
No of sputum sample tests	26.186	23.399	0	84	45*
No of audiology tests	2.7372	2.489	0	9	25*
No of U&E tests	26.186	23.399	0	84	22*
No of X-rays	2.8782	2.3537	0	9	220*
Meals consumed	1962	1,753.9	0	6275	25**
Urine dip stick tests	19.712	17.591	0	63	12*

Comments:

The general practice in KGH was to routinely request patient tests, and the following were common to the TB clinical setting.

a) **Laboratory Culture**

The purpose of conducting laboratory culture test was to confirm the diagnosis and identify micro-organisms causing the infection and susceptibility to antimicrobials. These tests were conducted by a contracted laboratory for the hospitals, and cost per test was R 120.00*. The table 4.11.1 indicated laboratory culture tests observed of 156 patients, with a mean of 5.64 tests conducted to average R 676.92 whilst in hospital. Maximum tests conducted per patient were 18 and at a cost of R 2,160.00 during the duration of stay in the hospital. The laboratory culture tests were deemed to be crucial to the medical practice as antimicrobial treatment are based on organisms cultured in the laboratory based on these results.

b) **Sputum Tests**

The purpose of conducting sputum test was to confirm diagnosis of TB, among other lung infections. The microscopic analysis of the sputum would also indicate the virulence of the infective agent. The number of sputum tests done on the 156 patients had a mean of 26.18; with average cost per patient of R 1,178.33, and 84 as the maximum sputum tests conducted for a patient costing R 3,780.00 during the duration of stay in hospital. In general the longer the patient stay in hospital the more the costs will be incurred due to tests and nursing care warranted.

c) **Audiology Tests**

The purpose of conducting audiology test was to assess the hearing ability of patients as TB medication especially streptomycin, can cause permanent hearing loss if not identified early. These tests conducted on 156 patients showed a mean of 2.74 and average cost per patient of R 68.43**,** with maximum tests conducted per patient as 9 amounted to R 225 for the duration of hospitalisation.

d) **Urine and Electrolytes (U&E) Tests**

The purpose of conducting U&E tests was to assess the patient's hemodynamic standing for consideration in treatment intervention. Number of U&E tests conducted showed a mean of 26.19, with average costs of R 576.07 and maximum tests for a patient hospitalised to be 84 costing R 1,848.00. This meant that long staying patient incurred more costs on tests.

e) **X-Ray Images**

The purpose of conducting X-ray test was to be used as a diagnosis tool and for assessing patient improvement on treatment interventions. The images depict the status of the lungs and infection progression. Of the 156 observed patients the mean of 2.88 tests per patient were conducted averaging at the cost of R 633.16; and maximum of 9 tests conducted for a patient costing R 1,980.00.

f) **Urine Dip Stick**

The purpose of conducting urine dip stick test as an initial screening test, when patients are examined for the first time, helps to assess any anomalies in patient's health, as infections could be detected by the increase in white blood cells, and glucose levels could also be used as a detection or screening for Diabetes Mellitus. The observed 156 patients had a mean of 19.71 dip stick tests with average cost of R 236.54; and maximum cost for a patient with 63 tests was R 756.00.

g) **Meals consumed**

The numbers of meals offered to hospitalised patients were 3 full meals and 2 snacks in a day. The meal cost for the longest stay patient was R 6,275.00. Hospital meals offered a balanced diet, and sufficient to patients nutritional requirements.

** Averaged Cost/Test Estimations: Price issued by the KGH Management Team*
X-Ray: R 220 / Test
Audiology: R 25 / Test
Meals Per Day: R 25 / Day
Laboratory Culture: R 120 / Test
Sputum Test: R 45 / Test
U&E Test: R 22 / Test
Urine Dip Stick: R 12 / Test

Table 4.11.2: Cost per Test averaged from 2002 – 2007, and stated in 2012 values

These tests as discussed are costs incorporated in the PDE calculations. The analysis of costs as separated, is to indicate the medical and non-medical cost portions that formulated the hospital XDR-TB expenditure in the calculation, in order to have an understanding of the type of examination costs covered.

4.12 DISTRIBUTION ON GENDER; HIV/AIDS; HEALTHCARE WORKER; HOSPITAL DISTRICT AND FINAL OUTCOME GROUP

Table 4.12.1: Gender Distribution

Gender	Patients	Percentage	Cumulative
Female	86	55.13	55.13
Male	70	44.87	100
Total	156	100	

Comments:

The study sample attracted 156 legible cases of which 86 were females at a 55.13% representation; whiles males were 70 at a 44.87% representation. The distribution is fairly common in most population, and one could attribute this to the general gender profile of many societies where there is a 1:3 ratio representation. Inclusion of gender comparison was to determine if there was a susceptibility of a specific gender to contracting TB. Mine workers in most cases are men and in some reports have shown to have higher chances of contracting TB due to occupational hazards. In this case such a conclusion cannot be made.

The condition of XDR-TB infection in gender profile only confirms the gender distribution on the study sample, and no claims on a particular gender that is prone to TB infection over the other.

Table 4.12.2: HIV/AIDS Distribution

HIV/AIDS	Patients	Percentage	Cumulative
Negative	37	23.72	23.72
Positive	106	67.95	91.67
Unknown	13	8.33	100
Total	156	100	

Comments:

The link between HIV/AIDS and XDR-TB is a major issue, with studies having concluded that HIV/AIDS had a huge impact on XDR-TB. Once someone is infected with TB it is reported that there is a 5-10% lifetime risk of developing the disease, but in a person with HIV/AIDS the risk is 5-15% a year (Wise, 2006).

In this scenario its clearly evident that of the 156 patients observed, 13 were of unknown status; 106 patients of 143 tested came out positive making it 74.13% infected, and 37 tested negative out of a total of 143 tested patients.

These results confirm what recent studies have concluded about the HIV/AIDS and XDR-TB link and a 67.95% out of 156 candidates in one hospital (i.e. KGH) having tested positive for both HIV/AIDS and XDR-TB is a major concern.

Cumulatively only 91.67% of the sample had an HIV/AIDS test conducted, with majority having tested positive for the virus.

Table 4.12.3: HealthCare Worker (HCW) Distribution

HCW	Patients	Percentage	Cumulative
NO	148	94.87	94.87
YES	8	5.13	100
Total	156	100	

Comments:

The concern about the increase in infectious disease in Africa also raised issues about a person's knowledge or general education. Table 4.12.3 attempted to determine if the career path in health does serve any benefit in living healthy, where treatable conditions could be avoided through healthy living.

The results indicates that 8 patients out of 156 (5.13%) were in a health related work environment, with 94.87%, 148 patients, with no health related employment records. In general, had there been more knowledgeable persons leading a healthy lifestyle, chances are that the XDR-TB incidence would be low.

Data on the healthcare workers observed had limitations on how the XDR-TB was contracted; and the HIV status of the HCW was not determined. No further conclusion could be made on HCW and XDR-TB association.

Table 4.12.4: Hospital District Patient Distribution

Hospital District	Patients	Percentage	Cumulative
Ugu (DC 21)	5	3.21	3.21
uMgungundlovu (DC 22)	18	11.54	14.74
Uthukela (DC 23)	4	2.56	17.31
Umzinyathi (DC 24)	50	32.05	49.36
Zululand (DC 26)	3	1.92	51.28
Umkhanyakude (DC 27)	5	3.21	54.49
Uthungulu (DC 28)	7	4.49	58.97
iLembe (DC 29)	2	1.28	60.26
Sisonke (DC 43)	1	0.64	60.9
eThekwini (DC 25)	61	39.1	100
Total	156	100	

Comments:

KGH serves as the only referral center for most of the TB related conditions in the KZN province, and parts of the Eastern Cape Province in SA. There was a total of 15 District Centers (DC) in the areas that utilised KGH services on TB treatment. The question of the emergence of XDR-TB in SA, and the mostly affected regions has been a topic of interest since 2005 with report from CoSH in the Umzinyathi district accounting for the highest number of reported cases.

eThekwini and the DC 24 have 39.10%, 32.05% of referred cases respectively in a sample of 156 cases. The reason for high numbers of cases emanating from the areas is due to close proximity to the referral site other that environmental factors. The sample size and study design is limiting in making claims beyond this.

In general the living conditions of patients had been noted to be unfavorable with no proper sanitation and communal living of many families in an informal settlement, and this has not changed to date. Such settings are breeding grounds for TB and other opportunistic infections.

Figure 4.12.1: KwaZulu-Natal Hospital Districts (KZN GIS unit, 2007)

Figure 4.12.1 indicates the location of hospital regions distribution within the province.

Table 4.12.5: Study sample Final Outcome Group Distribution

Final Outcome Group	Patients	Percentage	Cumulative
Beyond Study Analysis	73	46.79	46.79
Cured	1	0.64	47.44
Defaulted (known)	6	3.85	51.28
Died	57	36.54	87.82
Failed	4	2.56	90.38
Placebo Group (unknown defaulters)	15	9.62	100
Total	156	100	

Comments:

The final outcome observation analysed patients for a period of 12 months, in which a conclusion on each case is summarized as indicated in table 4.12.5 under the final outcome group column. The outcome conclusions were only recorded after each cycle of treatment was finalized per individual case, at times beyond the study focus period.

For the purpose of the study, a maximum of 365 days were assessed per individual case, which resulted in a total of 156 cases. It is imperative that an understanding on final outcome be understood, the conclusion is only done after 12 months of patient on treatment and a decision to allocate to a final outcome group will only be made thereafter.

This practice of assessing the patients after 12 months on treatment assist the medical practitioners in the hospital to gauge progress made in a 2 period cycle i.e. considering that initial phase take 2 months and continuous phase takes 4 months, and repetition of the cycle will take 12 months in total and assessment is then made to indicate as final outcome during that cycle(s) period.

Beyond Study Analysis: represent the conclusion of treatment outcome out of scope of the 365 days. In the study sample of 156 patients, 57 died within a year on treatment. Only 1 patient was considered cured of XDR-TB which represents a 0.64% success rate out of 156 patients. The odds of survival or cure when a patient is infected with XDR-TB are very low even less that 1%. This low survival rate could destabilize a nation should XDR-TB be allowed to spread to the /AIDS infected population.

Defaulters (known) and placebo group (unknown defaulters): a known defaulter is classified as such based on the requirements of the inclusion criteria. An unknown defaulter is termed a placebo group only for the purpose of using data for comparison. Unknown defaulters are patients that fake compliance whilst the recording sheets indicate otherwise.

4.13 INTERPRETATION OF RESULTS

The study results as determined through the tests conducted over a period of 6 years for the observations previously outlined also included cost of associated conditions. The study analysis used PDE to base the cost of caring for a patient in hospital, and also included parameters that determined costs breakdown based on the patient files examined.

Appendix 5 outlined the TB drug costs that were used to base medical cost determination, and non-medical costs were included as per hospital cost base methods which were not of scientific in nature but based on average estimation based on hospital guidelines.

Its paramount to note that considering the average costs in the study, there are similar findings on average cost of treating XDR-TB patients with SA Department of Health reported in 2006; although this study averages a 6 year period of a study sample of 156 patients and with a systematic approach to cost calculations, whilst the DoH's approach was rather medication based with very little consideration on detailed inpatients cost calculations.

Considering the PDE calculations on XDR-TB; the results indicate that caring for an XDR-TB patient in 2002 in real time 2012 value will cost R 77,404.00 per month (PDE of R 1,502.00) for the hospital. This is also consistent with the reviews made from studied literature were inter-and intra-district comparison with other similar hospitals were made.

Literature reviews on PDE, have indicated that the regions trend costs analysed over a period of four years (2006 to 2009) have indicated that variation in data could be due to inadequate quality of data or low PDE values where small changes could make a big difference to the cost per PDE (HST, 2009).

The average costs for twelve districts studied in SA resulted in PDE cost of R 964.00 in 2009 which at the time was recorded to be 12% below the SA average of R 1,096.00. The variations in PDE within regions is also due to differences in the number of district to regional hospitals within a region, as they attract different cost of labour (staff cost with fewer doctors or nursing personnel in senior post) or keeping patients in hospital for longer periods even when its due to difficulties with transporting them home.

In summary the PDE cost experienced at KGH is slightly above the SA average, when compared to other districts analysed through literature reviews. The reason for this could be due to staff expenditure, as more specialists attract high cost to the public sector, and the nature of how medical staffs conduct themselves and manage resources in their hospital.

CHAPTER 5

5. CONCLUSION

The study findings has managed to analyze the cost involved in treating an XDR-TB patients, though there are varying elements involved with inpatients and out-patients.

The ideal situation in managing XDR-TB patient is to have them isolated in hospital or in a ward designated for TB sufferers. In KGH setting, due to lack of resources, only severely immobile patients are hospitalised, and once there is a sign of improvement patients are then discharged. There are cases were patients with TB, MDR-TB and in some instances XDR-TB patients are sent back in the community due to lack of bed space in hospital. This study project however was not tasked to investigate on such matters, rather on costs in caring for XDR-TB patients.

The costs of XDR-TB having utilised the PDE analysis for a 30 day treatment cost, indicates an annual increase in treating a patient costing R 77,404.00 in 2002, and escalating to R 144,221.00 in 2007, stated in 2012 value terms. In the year studied, day patients' days decreased annually whilst the inpatient days increased sharply resulting in an increase on total hospital expenditure. Results also indicated a directly proportional increase in medical costs with inpatients days by R 201.04 per day spent in hospital. The total costs increased at the rate of R 511.16 for each day the patient was on XDR-TB treatment, and associated conditions.

The costs of PDE in KGH are consistent with literature cost experienced in studies conducted in 2006 to 2009, although we have experienced that KGH have an above PDE than the average of the SA district studied. This leads us to acknowledge that hospital management is investing resources in managing the specialised TB hospital facility, as costs of specialists within the facility had a bearing in slightly increased PDE above the average SA figure, as stated. Although the initiative made by the KGH hospital to outline a treatment protocol, for XDR-TB when no organization in the country had any knowledge of how to deal with XDR-TB is a good sign of management that is geared to deal with the condition, and this shows in the reporting process of the cost of XDR-TB and data capturing. The inclusion of XDR-TB in the essential drug list was motivated by the successful use of medication in the KGH to treat the condition.

The extrapolation of XDR-TB from the total hospital expenditure graph is consistent with the constant increase in the cost of treating the condition on an annual basis.

Investigation on associated link between HIV/AIDS infection and XDR-TB vulnerable patients indicated that 106 patients tested positive from a total of 143 consented patients to testing. This gives an average of 74.13% of patients that have XDR-TB have HIV/AIDS as well.

The costs of treatment for inpatients had a directly proportional increase to hospital stay, whilst average hospital days were noted to be 78 days (i.e. two months and three weeks). Outpatient's days on treatment were noted to be on average 105 days (i.e. three months and two weeks).

Information gathered during the project on cost involved in treating XDR-TB, has made it evident that this study only touched the surface on the national crisis loaming should XDR-TB not be prevented from spreading. As mortality and morbidly rate with XDR-TB is usually high due to low success rate because of non-compliance, and exposure to a single drug, inappropriate prescription, irregular drug supply or poor drug quality (Frazer *et al.*, 2006).

The secondary objective of the study hopes to initiate some form of debate or critic on XDR-TB costs and spend allocation on curbing the disease.

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ANNEXURE 1

- Drug Dosage for MDR-TB in KZN Province

No	Drug	33 - 50 Kg	51 - 65 Kg	> 65 Kg
1	Parazinamide	1 g	1.5g	2 g (2.5 g max)
2	Amikacin/Kanamycin	500 mg - 750 mg	750 mg - 1 g	1 g
3	Ethionamide	500 mg	750 mg	750 mg (1g max)
4	Ofloxacin	800 mg	800 mg	800 mg
OR	Ciprofloxacin	1.5 g	1.5 g	1.5 g
5	Ethambutol	800 mg	1.2 g	1.6 g (2 g max)
AND	Terizidone or Cycloserine	250 mg bd	250 mg tds	250 mg tds (1 g max)

ANNEXURE 2

- Drug Dosage for XDR-TB in KZN Province

Drug	33 - 50 Kg	51 - 65 Kg	> 65 Kg
Parazinamide	1 g	1.5 g	2 g (2.5 g max)
Ethambutol	800 mg	1.2 g	1.6 g (2 g max)
Terizidone or Cycloserine	250 mg bd	250 mg tds	250 mg tds (1 g max)
Ethionamide	500 mg	750 mg	750 mg (1 g max)
Para-aminosalycilic acid (PAS)	4 g bd	4 g bd	4 g bd
Capreomycin	500 mg - 750 mg	750 mg - 1 g	1 g
Only if Capreomycin or PAS are not tolerated, then add the following two drugs			
Clarithromycin (Klacid®)	500 mg bd	500 mg bd	500 mg bd
Augmentin®	2 g bd	2 g bd	2 g bd
Klacid® and/or Augmentin® only added should PAS and/or Capreomycin not be tolerated			

ANNEXURE 3

- Standardised TB Treatment by DoH - SA

Regimen 1 New cases with age above 8 years and adults

New smear-positive and new smear-negative patients with pulmonary and extra pulmonary TB:

Pre-treatment Body Weight	Two months initial phase given five times a week	Four times continuation phase When given five times a week	
	RHZE (150/75/400/275) mg	RH (150/75) mg	RH (300/150) mg
30 - 37 Kg	2 tablets	2 tablets	
38 - 54 Kg	3 tablets	3 tablets	
55 - 70 Kg	4 tablets		2 tablets
71 Kg and over	5 tablets		2 tablets

Regimen 2 Re-treatment cases

Previously treated TB patients after cure, completion, interruption and /or failure:

Pre-treatment Body Weight	Two months initial phase Given five times a week		3rd month initial phase given five times a week	Five months continuation phase When given five times a week			
	RHZE (150/75/400/275) mg	Streptomycin	RHZE (150/75/400/275) mg	RH (150/75) mg	E (400) mg	RH (300/150) mg	E (400) mg
30 - 37 Kg	2 tablets	500 mg	2 tablets	2 tablets	2 tablets		
38 - 54 kg	3 tablets	750 mg	3 tablets	3 tablets	2 tablets		
55 - 70 kg	4 tablets	1 g	4 tablets			2 tablets	3 tablets
71kg and over	5 tablets	1 g	5 tablets			2 tablets	3 tablets

Fixed dose drug combinations available:

RH-150/75 mg	RH - 300/150 mg
RH-150/150 mg	RHZE - 150/75/400/275 mg
R - Rifampicin	**H** - Isoniazid (INH)
Z - Pyrazinamide	**E** - Ethambutol

ANNEXURE 4

- Approval Letter to Access Patient Records from Church of Scotland Hospital by Chief Executive Officer

HEALTH
KwaZulu-Natal

CHURCH OF SCOTLAND HOSPITAL
Private Bag x 502
Tugela Ferry, 3010
Tel.: 033 – 4930004 ext. 3332, Fax.: 033 - 4930828
Email.: hans.human@kznhealth.gov.za

Reference :
Enquiries : H.J. Human
Telephone : 033 – 4930004 ext. 3332
Date : 9 July 2007

WITS Senate
The University of the Witwatersrand
Faculty of Health Sciences
School of Pharmacy
Parktown

Dear Sir/Madame

PERMISSION FOR A RETROSPECTIVE ANALYSIS OF EXTENSIVE DRUG RESISTANT TUBERCULOSIS INVESTIGATING THE PHARMACO-ECONOMICAL IMPACT AT THE CHURCH OF SCOTLAND HOSPITAL IN KWAZULU-NATAL, SOUTH AFRICA.

Permission is hereby granted to Mr. Lebogang Molobi to perform the said retrospective study at the Church of Scotland Hospital, provide that he comply to the prescripts and requirements of the Ethics Committee of your institution.

Should you need any further information please contact the undersigned.

Yours faithfully.

H J HUMAN
CEO: CHURCH OF SCOTLAND HOSPITAL

ANNEXURE 5

- Approval Letter to Access Patient Records from King George Hospital by Medical Manager

JUL.25'2007 13:12 0312099586 KGV MANAGEMENT #3091 P.001/001

DEPARTMENT OF HEALTH
PROVINCE OF KWAZULU-NATAL

KING GEORGE V HOSPITAL

PO DORMERTON,4015
75 STANLEY COPLEY DRIVE, SYDENHAM, DURBAN

Enquiries	: Dr S Maharaj	Telephone Number Extension	: (031) 2087121 : 356	Fax Number	: (031) 2099586
Email	:shamin.maharaj@kznhealth.gov.za	Your Reference	:	Date	: 20 July 2007

Mr Lebogang Molobi
Pharmacy Student
Witwatersrand University
FAX 0866871718
Dear Mr Lebogang Molobi

REQUEST FOR PERMISSION - ACCESS TO PATIENT INFORMATION AT KING GEORGE V HOSPITAL

1. Your letter dated 16 July 2007 refers.

2. Permission is granted for the above mentioned purpose. Please find attached copy of indemnity form for completion and submission by each student prior to undertaking the study.

3. Your attention is once again drawn to the maintenance of confidentiality as discussed.

4. Arrangements should be made for you to work with patients and staff in the MDR TB Department.

S Rmaharaj

DR S B MAHARAJ
MEDICAL MANAGER

APPENDIX 1

- Code Reference Formula

CODE REFERENCE FORMULA

Hidden Details	Code Referencing Key	Patient File Number
Patient Hospital Number	**X -** Female	As prescribed
	Y - Male	
	K - King George	
	CH - CoSH	
	A - Active/XDR-TB Patient	
	B - Control Patient	
	Z - TB/MDR-TB Patient	

A/B/Z : to be denoted at the end of each number

	Circle Appropriate Location	
Patient File Number	**King George Hospital**	**Church of Scotland**
1	XK 200800001 YK200800001	XC200800001 YC200800001
2	XK 200800002 YK200800002	XC200800002 YC200800002
3	XK 200800003 YK200800003	XC200800003 YC200800003
4	XK 200800004 YK200800004	XC200800004 YC200800004
5	XK 200800005 YK200800005	XC200800005 YC200800005
6	XK 200800006 YK200800006	XC200800006 YC200800006
7	XK 200800007 YK200800007	XC200800007 YC200800007
8	XK 200800008 YK200800008	XC200800008 YC200800008
9	XK 200800009 YK200800009	XC200800009 YC200800009
10	XK 200800010 YK200800010	XC200800010 YC200800010
11	XK 200800011 YK200800011	XC200800011 YC200800011
12	XK 200800012 YK200800012	XC200800012 YC200800012
13	XK 200800013 YK200800013	XC200800013 YC200800013
14	XK 200800014 YK200800014	XC200800014 YC200800014

APPENDIX 2

- **Data Collection Form**

DATA COLLECTION FORM

Date : _____
Completed : _____
Completed (Name) : _____

Participant No.	_____					
Hospital No.	_____					
Gender	Male		Female			
Age	> 18 - 24		25 - 35	36 - 45	> 45	
Weight	.....Kg					
Date of initial diagnosis of TB	/ /	DD/MM/YY				
Date of initial diagnosis of MDR-TB	/ /	DD/MM/YY				
Date of initial diagnosis of XDR-TB	/ /	DD/MM/YY				
Participant on TB therapy?	Yes		No	Start Date	/ /	DD/MM/YY
Stop date of TB therapy	/ /	DD/MM/YY				
Resume date of TB therapy	/ /	DD/MM/YY				

Appendix 2: Data Collection Form

Participant on MDR-TB therapy? Yes No Start Date / / DD/MM/YY

Stop date of MDR-TB therapy / / DD/MM/YY

Resume date of MDR-TB therapy / / DD/MM/YY

Participant on XDR-TB therapy? Yes No Start Date / / DD/MM/YY

Stop date of XDR-TB therapy / / DD/MM/YY

Resume date of XDR-TB therapy / / DD/MM/YY

Date of Hospitalization / / DD/MM/YY

Date of death / / DD/MM/YY

No. of meals taken daily <2 3 4 >4

Participant on ARV therapy? Yes No Start Date / / DD/MM/YY

Stop date of ARV therapy / / DD/MM/YY

Resumed date of ARV therapy / / DD/MM/YY

Stage of RVD (CD4 count) 1 2 3

Was ARV therapy successful? Yes No Successful therapy is CD4 > 500 cells/µL

Compliance to ARV therapy? Yes No

Any co-infections? Yes No

Was TB therapy successful? Yes No

Was MDR-TB therapy successful? Yes No

Was XDR-TB therapy successful? Yes No

Was there TB relapse? Yes No

Was there MDR-TB relapse? Yes No

Was there XDR-TB relapse? Yes No

OTHER COSTS ATTACHED TO TREATMENT

Consumables (Indicate items used)	Price
Accommodation	**Tariff**
Normal Ward	
ICU	
High Care	
Isolation ward	
Professional Fees (standardized fee by The State, on consultation)	**Fee**
Initial Visit	
In Hospital visit	
Follow up visit	

APPENDIX 3

- Staff Information Form

STAFF INFORMATION FORM

STUDY TITLE: A retrospective cost analysis investigation of the extensive drug resistant tuberculosis treatment at the Church of Scotland Hospital in KwaZulu-Natal, South Africa.

INVESTIGATOR: Lebogang Molobi

PROTOCOL DATE: 20 February 2008

AMENDMENT DATE: March 2008

Good Day

Dear Sir/Madam

INTRODUCTION

I am a Masters candidate from the University of the Witwatersrand and am interested in investigating treatment costs of Extreme Drug Resistant Tuberculosis (XDR-TB) at this Hospital.

INVITATION TO PARTICIPATE

You are requested and invited to offer assistance and cooperation regarding the study on Extreme Drug Resistant Tuberculosis. Before you agree to assist, you should fully understand that the study does not involve your state of health but of those that the hospital treats on a monthly basis, and you are requested to treat all aspects of the study as confidential.

THE OBJECTIVE OF THE STUDY

We are embarking on a study that seeks to learn about the costs involved in treating an Extreme Drug Resistant Tuberculosis patient at this Hospital.

The study is anticipated to take not longer than 4 weeks were your direct involvement will be requested.

Patient charts will be the focal point of the study were each patient's treatment will be studied in detail to calculate the costs that the hospital has incurred for that particular patient in a 10 months period. This information will be compared with a group of non-XDRTB patients for thorough assessment

YOUR INVOLVEMENT

Your role in the study entails cooperating with the investigator, and assisting by sharing information were needed for costing the treatments that have been offered to patients.

You will not be exposed to patient names, as patient confidentiality will be maintained. However, patient charts will be code referenced in order for costs to be attached to the correct patient chart.

You will not be expected to perform the investigator's work as this projected will not offer you any form of monetary compensation.

Your daily duties for the Department of Health will always take top priority where the investigator requires your assistance.

POSSIBLE RISKS AND BENEFITS OF PARTICIPATION

We do not expect any potential risks involved with the study, and your health as explained before, is not of direct interest to the study.

The expected benefits for all involved in the project will be self-fulfillment of a task well completed in the advancement of XDR-TB education.

CONFIDENTIALITY

All medical researchers are expected to have a signed consent for study participation in order to ascertain proper ethical principles are adhered to. You are requested in this regard to sign consenting to the above information, and to cooperate with the investigator. You are also requested to treat any matters arising from the study in confidence.

Should you require further details, kindly contact the investigator on 082 565 3373 (24hrs).

Thank You

Lebogang Molobi
Investigator

APPENDIX 4

- **Staff Confidentiality and Consent Form**

STAFF CONFIDENTIALITY AND CONSENT FORM

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You will not be expected to perform the investigator's work as this projected will not offer you any form of monetary compensation.

Your daily duties for the Department of Health will always take top priority where the investigator requires your assistance.

POSSIBLE RISKS AND BENEFITS OF PARTICIPATION

We do not expect any potential risks involved with the study, and your health as explained before, is not of direct interest to the study.

The expected benefits for all involved in the project will be self-fulfillment of a task well completed in the advancement of XDR-TB education.

CONFIDENTIALITY

All medical researchers are expected to have a signed consent for study participation in order to ascertain proper ethical principles are adhered to. You are requested in this regard to sign consenting to the above information, and to cooperate with the investigator. You are also requested to treat any matters arising from the study in confidence.

CONSENT FORM

I .....agree to participate and cooperate with the investigator on all matters involved with the study discussed above. The investigator has taken time to explain to me how I will be of assistance to him. I fully understand my role in the study. I am also aware that I can withdraw from assisting the investigator without offering any reason and being victimized.

Signature: ……

Date: ……...

Place: ……..

APPENDIX 5

- **Drug Price List (TB)**

Drug Pricing (DoH)		
	2007	2012
Drug Name	**Cost Per Month**	**Cost Per Month**
Amikacin 1g (5x)	400.00	585.00
Amo/Clav 1g BD	178.00	210.00
Capreomycin 1g (5x)	1 658.00	1 742.00
Ciprofloxacin 1.5g D	36.00	44.00
Clarithromycin 500mg BD	228.00	130.00
Cycloserine 250mg TDS	820.00	795.00
Ethambutol 1.2g D	43.00	38.00
Ethionamide 1g D	111.00	88.00
Ofloxacin 800mg D	57.00	124.00
Parazinamide 1.5g D	42.00	51.00
PAS 4g BD	1 640.00	1 520.00
Rifafour e-275 (4 BD)	74.00	64.00
Rifinah 300 (2 BD)	44.00	41.00
Streptomycin Sulphate 1g	7.00	5.00
Terizidone 250mg TDS	641.00	662.00
Other:		
Paracetamol 500mg TDS	10.00	8.00
Fungizone 1 BD	120.00	150.00
Betadine gel	30.00	36.00
Ibuprofen 400mg TDS	15.00	12.00
Vitamin C 100mg TDS	6.00	5.00
Vitamin B Complex 2 BD	4.00	4.00